TRANSACTIONS OF THE AMERICAN CONGRESS ON INTERNAL MEDICINE 1916

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TRANSACTIONS

OF THE

AMERICAN CONGRESS

ON

INTERNAL MEDICINE

FIRST SCIENTIFIC SESSION, NEW YORK CITY
DECEMBER 28—29, 1916

EDITED BY
HEINRICH STERN

ASSISTED BY
EDWARD E. CORNWALL

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CONTENTS

PAGE

List of Officers 3

Address of Welcome by Thomas E. Satterthwaite 7

Response to Address of Welcome, by Charles D. Aaron 8

Address of President, Reynold W. Wilcox 9

Discussion of the President's Address, by L. F. Bishop, J. C. Hemmeter, C. E. de M. Sajous, W. B. Stewart, W. H. Mercur, Briggs, R. H. Babcock and J. Diner 22

Report of the Secretary-General, Heinrich Stern 24

Report of the Treasurer, Augustus Caillé 27

Obituaries of P. B. Porter and F. H. Daniels, by L. F. Bishop. 27

Officers elected for ensuing year 29

The Ductless Glands in Cardiovascular Diseases and Dementia Precox, by Charles E. de M. Sajous 30

Cardiovascular Diseases and the Ductless Glands, by Judson Daland 49

Dementia Praecox and the Ductless Glands, by Francis X. Dercum 54

Discussion of the papers on Ductless Glands, Cardiovascular Diseases and Dementia Praecox, by Harlow Brooks, S. E. Jeliffe, Robert H. Babcock, Ernest Zueblin, Tom Williams, Francis X. Dercum and C. E. de M. Sajous 61

The Diagnosis of Duodenal Ulcer, by John B. Deaver 72

The Prognosis of Duodenal Ulcer, by Max Einhorn 78

The Possible Dependence of Gastro-Duodenal Ulcer Upon a Disturbance of Internal Secretion, by Gedide A. Friedman 80

Venous Stasis and Colloidal Diffusion as Etiological Factors of Gastro-Duodenal Ulcer, by Fenton B. Turck 94

Discussion of Gastric and Duodenal Ulcer, by J. C. Hemmeter, I. Kaufmann, G. Lenox Curtis, J. R. Verbrycke, J. W. Weinstein, W. J. Mallory, W. H. Stewart, M. Gross, G. A. Friedman and F. B. Turck 103

TRANSACTIONS OF THE AMERICAN CONGRESS ON INTERNAL MEDICINE, FIRST SCIENTIFIC SESSION

DECEMBER 28-29, 1916,
HOTEL ASTOR, NEW YORK

The Congress was called to order at 11 A. M., December 28, 1916, by the President, Dr. Reynold Webb Wilcox.

The President called on Dr. Thomas E. Satterthwaite, of New York, to welcome the out-of-town members.

Dr. Satterthwaite: On behalf of the New York members, we welcome you all, from various parts of the country, to this first meeting of the American Congress on Internal Medicine, the sessions of which begin now and last to-day and to-morrow.

A good many of us have felt that there is great need for a congress of this kind, and the number of men who have joined is an index that we were correct in that respect. The proceedings of to-day will begin with an address by our President, Dr. Wilcox, and I will say that we should be very glad that Dr. Wilcox is our President, because he is one who will organize the congress in a way that will make it a success.

Following the President's Address, we shall have a paper on "The Ductless Glands in Cardio-Vascular Diseases and Dementia Precox," by Charles E. de M. Sajous, who as we all know, is an authority on this subject.

Then we shall take up the subject of Duodenal Ulcer, and John B. Deaver, of Philadelphia, the great authority on surgical diagnosis, will be the first to speak, and he will be followed by Max Einhorn, Gedide A. Friedman and Fenton B. Turck, of this city.

Gentlemen, I will say no more, as there is a great deal before us to do. I hope that we shall have a very successful meeting, and I am quite sure that we shall.

The President called on Charles D. Aaron, of Detroit, to respond for the out-of-town members.

Dr. Aaron, of Detroit: On behalf of the out-of-town members, I would say that we appreciate greatly the privilege of being here to meet the more prominent internists in New York and its vicinity. By their very presence here the out-of-town members show their appreciation of the invitation extended to them to be with you to-day.

Great credit should be extended to the officers and councillors of the American Congress on Internal Medicine for the enormous amount of work which they have done in laying the foundation for this great enterprise. The out-of-town members realize more than they can express that an association of this kind is more important to them than it is to the physicians of New York. It is important that the internists of the United States should come forward in their effort to raise the standard of medicine, and the out-of-town members realize more than ever that it is only by co-operation in the way that the officers and councillors have started this Association, that the standard and recognition of internal medicine will be made greater than it ever has been, and that the laity will be taught to appreciate the internist equally as well as the surgeon. I can tell you a story, gentlemen, of an incident that took place in my own city this present year. There was a woman, who with her son, came from St. Louis to Detroit and went to a summer resort up the river. Her son was taken down with typhoid fever. Immediately the wife wired her husband at St. Louis to know what physician in Detroit it was advisable for her to consult for the care of that typhoid fever case. The husband made inquiry in St. Louis and found that the most prominent physician in Detroit was a surgeon, and he wired to his wife, "Call on Dr. So and So," naming one of our prominent surgeons. She took the telegram, walked up to the clerk of the hotel and said, "Do you know Dr. So and So?" The clerk said, "I certainly do." "Is he a good physician?" The clerk said, "One of the very best." She went to some other Detroiters and asked the same question, and they all said he was the very best. She immediately telephoned to the surgeon that she was coming to Detroit with this invalid, her son. The surgeon met the typhoid patient with an ambulance and took him to the hospital. He said: "What can I do? The husband demands this from St. Louis. The people here demand it. They feel as though the whole recovery of this typhoid fever case depends upon me. If I turn this case down, it is going to be a disappointment to them all, and so I must keep it." Gentlemen, I hope that the Congress on Internal Medicine will do

something to prevent things of that sort; and I hope that this initial movement will be crowned with great success. I do not want to take too much time, but I could say a great deal more. However, we feel convinced that this movement, thus started, is just what we desire.

The President asked the Vice-President, Dr. E. H. Bartley, to take the chair.

The President, Dr. R. W. Wilcox, read the following address:

THE FIELD OF INTERNAL MEDICINE

By REYNOLD WEBB WILCOX,
New York

It is an occasion of more than ordinary importance when the American Congress on Internal Medicine convenes for its second annual meeting, which is, however, its first scientific session. It has completed its physical organization and now presents its scientific programme. Its organization marks a new era in American medicine, and the programme which has been chosen determines a new standard for scientific work in the profession of which we are the exponents.

The organization of this Congress does not signify the differentiation of a new specialty, but the delimitation of the oldest branch of the healing art, for it is probable that disease received earlier attention than injury. Whatever may be the fact, it is, however, true that medicine and surgery were yet undifferentiated in practice throughout the era of the prehistoric man, and even for many centuries thereafter. As war became more and more an organized operation and campaigns were planned, the care of the wounded devolved upon the practitioner of the healing art, and surgery became differentiated in name as well as practice, and the chief surgeon of the army was often the physician of the ruling prince or king. Nor, indeed, did his professional title always change, for even so late as the War of the Revolution in this country the title of the medical officer was physician and not surgeon. Yet today in the army the title of surgeon prevails, while the more important work of the military practitioner, whether considered from the combatant or the altruistic standpoint, is medical rather than surgical.

What then is the domain of internal medicine? Shall we define it as what remains after surgery and the narrower specialties,

as ophthalmology, otology, laryngology, gynecology, andrology and urology, or whatever of it belongs to the preceding two categories, are subtracted? Or shall we still further diminish its field by eliminating neurology, psychiatry, pediatrics and dermatology? The position of the dermatologist calls for especial consideration. It is conceded that surgery does not claim him. If we follow the Vienna school in assuming that the skin is an organ, as the eye or the ear, he would be an exponent of one of the narrower fields of specialism. If we should adhere to the tenets of the London school and expect the attention to be directed to the study of systemic conditions, which that school has emphasized, he could readily be enrolled as a practitioner of internal medicine. In fact, one of the greatest names of that department of the healing art was Hutchinson, whose fame rests largely upon a disease, syphilis, which is clearly in the field of internal medicine. If we are influenced by the Paris school, our decision must rest somewhat in doubt. However, this is a question upon which the Congress eventually must take official action. A definition which is predicated solely upon exclusion is neither logical nor final. The schismatic operations being repeated, the remaining moiety might readily become negligible. A definition must be not only inclusive, but as well exclusive. We may define the domain of internal medicine as including:

1. Diseases caused by parasites: Psorospermiasis, distomiasis, trypanosomiasis and by nematodes, cestodes and parasitic insects from arachnidæ to pediculi, either as directly causing disease or by their acting as carriers.

2. Infectious diseases, of which enteric fever, diphtheria, infectious pneumonia, tuberculosis, erysipelas, syphilis and the eruptive fevers, communicable or contagious, represent various types. These number nearly ninety, the majority of definite and known causation, all readily recognizable, and all presenting pathological manifestations of which the treatment must fall to the lot of the internist.

3. Constitutional diseases, such as gout, diabetes, scurvy, rickets and others.

4. Intoxications, including the various metallic poisonings, alcoholism and other drug poisonings, food and occupational poisonings, and the results of exposure to high temperatures.

5. Diseases of the digestive system and its adnexa, the liver, and pancreas.

6. Diseases of the blood and of the ductless glands, which are not only of increasing interest and importance, but are likely, in the future, to necessitate a new classification.

7. Diseases of the circulatory system: heart, pericardium and blood vessels.

8. Diseases of the respiratory system, including those of the pleura.

9. Diseases of the mediastinum, few in number, and relatively rare, but of enormous difficulty in diagnosis.

10. Diseases of the urinary system.

11. Diseases of the nervous system, including those of the mind.

12. Diseases of the muscular system; the myosites, the dystrophies and the disorders of function of which myasthenia, myotonia and paramyoclonus are types.

It cannot be assumed that this classification is final, because not only are individual diseases constantly changing from one division to another, as, for instance, pneumonia from diseases of the respiratory system to the infectious diseases, but also some groups may be merged together as our knowledge of etiology increases. The terrain will remain the same, although the boundaries of the different divisions may change.

This, then, is the broad domain of internal medicine; which is of such eminent importance in the life-history of mankind, and which dominates all the limited specialties of the healing art. Its successful cultivation demands that all sciences render aid—physics, and its younger brother, physical chemistry, botany, zoölogy and especially biology in the broader acceptation. Upon this advanced knowledge and the logical interpretations of it, and the legitimate applications to that complex category of physico-chemical relationships, which we call life, must depend substantial and beneficial progress in internal medicine. In its domain are to be found the greatest incidence of disease, either in number or importance of disability and the preponderating causes of death.

Can this field of internal medicine be divided? There is no doubt that in practice this may be done to a limited extent. For instance, diseases of the nervous system can be separated from internal medicine and the neurologist may confine his efforts to diseases of that system, and further the psychiatrist may limit his practice to the diseases of the mind, but he will be the more useful alienist whose knowledge of diseases of the nervous system is the greater, and both will be more completely experts the more accurate

and comprehensive their knowledge of the broad field of internal medicine has become. The medical diseases of infancy and childhood have many exponents who properly confine their practice to those periods, because not only does the physiology and pathology of the constructive period of the body differ from that of the adult, but diagnosis and treatment present variant problems. So also do the diseases incident to old age, but with a solution hopeless as to the final outcome, though fruitful in alleviating many of its discomforts. In passing, attention might be called to the fact that the time during which the pediatrist exercises his functions does not always end with puberty, but may even extend itself through that of childhood, which some of our pedagogues, notably college presidents, assume to continue during the entire period of education which is necessary to adapt the human being to his environment and to fit him for his greatest usefulness, and this period has been mentioned as thirty years. When we reflect that the storm and stress of modern civilization have shortened the span of human life, and men may be octogenarians in body, if not mind, at sixty or even earlier, the period of adult life may become a brief one, and the pediatrist and the geriatrist may almost meet in their separate fields of activity. Thus it is evident that both should be thoroughly versed in the domain of internal medicine. It is indeed true that the foundation of senility is laid in the period of childhood, and that man usually begins to die the moment that he is born. The laboratory workers, whether in the field of biological chemistry, bacteriology, parasitology, physiological therapeutics and in physics, especially in electro-therapeutics and röntgenology, certainly have claim upon our consideration. To them internal medicine owes much, not only in indicating new avenues of progress, but as well in scientific demonstration of the verity of what empirically we have established as facts in internal medicine, and we have made but a beginning.

Granting that the foregoing are legitimate subdivisions of scientific endeavor and practical realization in the field of internal medicine, the question of further limitation of practice immediately suggests itself. The natural cleavage would be in accordance with the classification which has been given at the outset, according to the different physiological systems. The diseases of the circulatory system depend upon a distinct group of organs, but the results of imperfect function or structural disease are as far reaching as the circulation of the blood, and their symptomatology may be the

symptoms ascribable to any one, many, or all of the physiological systems. The worker in the field of diseases of the circulatory system may limit his practice, but he will be expert only as he is versed in internal medicine. The stomach specialist *per se* has no reason for his existence. If he devotes himself to diseases of the digestive system and includes with these the disorders of metabolism and the constitutional diseases, his field is broad enough to occupy his best endeavors, but here again he must be conversant with the established facts of the larger territory occupied by internal medicine if he shall attain real usefulness.

So might be cited the group of infectious diseases, often presenting problems of diagnosis, and the same statement applies as to the importance of a broad and comprehensive knowledge of internal medicine. Further than this, the exponent of internal medicine, no matter whether he shall be the one considering the field in its entirety, or one limiting his work to a subdivision of it, must know syphilis in all its manifestations, and its results. For its widely spread incidence must always be taken into account as modifying disease or dominating therapy throughout the whole field of internal medicine. Its signs and symptoms are often so bizarre that even its recognition, at times, is exceedingly difficult, the Wassermann reaction notwithstanding. The range and scope of internal medicine are well defined and its domain is accurately marked out, both inclusively and exclusively.

The relationship of surgery to internal medicine is intimate, and yet the differentiation is apparent. There is hardly a disease in the entire range of internal medicine but that at some time in its course, or in the presence of some complication, surgical intervention may be called for. And this intervention may be necessary at an early date—in fact, so soon as the diagnosis can be established, as, for instance, in acute appendicitis. It is well to bear in mind that what are often denominated border-line diseases are really those in which the activities of the medical attention and surgical practice are concurrent. There are others, for example, cholelithiasis, in which the etiology falls in the domain of internal medicine, the important item of relief comes under the jurisdiction of the surgeon, while the final cure comes within the purview of internal medicine.

As internal medicine and its contributing laboratory work has laid the foundations for real surgical advance, so internal medicine can make surgery of its highest possible value. The best surgical

work done in this country to-day is accomplished by intimate scientific coöperation between the skilled exponents of internal medicine and the expert operator. The mere operator may be an agent of destruction, no matter how deft he may be or how perfect his technic. He only reaches his highest usefulness when he has a broad knowledge of internal medicine; that is, becomes a surgeon, or relies upon other experts for diagnosis and an analysis of the real condition of the organs and functions of the patient. Naturally, this statement does not apply in its entirety to operations of urgency. When the surgeon attempts to be a general practitioner we are likely to be informed as to the surgery of dyspepsia or the ablation of a function. Medical surgery is not likely to yield the best results and surgical medicine is sure to be disappointing.

The relationship of internal medicine to surgery is fundamental and necessary—this fact must be recognized by the practitioners of both—but it must be founded on mutual confidence and respect for technical skill. Although internal medicine dominates the situation, it does not detract from a just admiration for the wonderful results which modern surgery has accomplished. The mechanical skill and the perfect technic of the operator are rewarded by appreciation, but the intellectual work of the trained exponent of internal medicine is equally worthy of admiration.

We have defined the field of internal medicine and have shown its relationship to the coördinate branch of the healing art—surgery —and the narrow specialties, and now we must define our name. It is a curious fact that the practitioners of internal medicine have not yet, by common consent, so far as this country is concerned, received a distinctive name. The term "diagnostician" has been suggested. Diagnosticians we certainly are, and we are proud to be considered as such, but we realize, better probably than any other group of practitioners, that diagnosis is not the sum total of our efforts, but only the conclusion of the first stage of our work, and merely preliminary to the part that is most important to our patients, which is treatment. We certainly are not general practitioners, either in theory or practice. For, with the mass of accumulated facts and the logical deductions therefrom, neither the learning of an Aristotle nor the intellect of a Bacon, nor both combined, if such a genius were possible, could result in so broad a knowledge, so vast an experience, and so great a technical skill that all phases of scientific endeavor could be marked with such a degree of usefulness as we believe adequate for professional work.

Nor does this statement conflict with the opinion that specialists, both broad and narrow, are better specialists if the earlier years of their career are devoted to general practice, and the broader their knowledge and the larger their experience in the general field the more likely are they to become really expert in the smaller field to which their natural aptitude or especial opportunities may have limited them. The name "internist" is undoubtedly the proper one for those whose activities are circumscribed by the limits which have been set down earlier in this address. The term "physician" too often is assumed to have the qualifying adjective "general" omitted, and is not distinctive. In the profession, even, one who has worked exclusively in the field of internal medicine for a quarter of a century, eschewing surgery, obstetrics and the narrower specialties, who has been a teacher of medicine and an author of text-books upon its practice, is frequently and erroneously designated as a "general practitioner." In Great Britain we are known as "internists"; on the Continent "internal medicine" is recognized; let us be known in this country as internists, and be willing to define the term until such time as the profession and the people know what it means, and medical associations, big and little, representing or not medical science, afford the designation official recognition. We must teach that the "internist" is an educated and trained physician, who gives his best endeavors to an accurately delimited field, known as "internal medicine," and that the real internist is not only a specialist, but, what is far more rare, an expert. It is to the internist that the heritage of the earlier physicians has come. This is the American Congress on Internal Medicine, and we are the descendants of men who have served their time and generation, and have left their impress upon American medicine.

We probably recall John Morgan (b. 1736), of Philadelphia, pioneer with William Shippen, Jr. (b. 1736), in the establishment of a school for medical education, the grandfather of American medicine, and Samuel Bard (b. 1742), of New York, who was identified with the earliest medical instruction in this city. Probably the best known name of this generation, but whose activities were so varied that he is better known in connection with the revolutionary period, was the Father of American Medicine, Benjamin Rush (b. 1745), of Philadelphia; his third edition of "Medical Inquiries and Observations Upon the Diseases of the Mind" (his first was in 1812) lies before me bearing the date 1827. It is inter-

esting; if not instructive, and is written in idiomatic and classical English well worthy of Addison, and it is a model for the medical editor of today.

Another worthy of this period was Nathan Smith (b. 1762), who at Dartmouth did not occupy a professional chair, but rather an entire settee, for he taught medicine, surgery, anatomy, therapeutics, botany, physiology and chemistry. A contemporary of Daniel Webster, although there was twenty years difference in their ages, he contributed much to medical science, as well as established two medical schools. In 1813 he came to New Haven and repeated his pioneer work in founding the medical school which subsequently became a part of Yale. He died in 1829, and his grave in the Grove Street cemetery is still a Mecca for medical men. As professor of the theory and practice of physics and surgery, his name is upon my grandfather's diploma, in 1819.

The fourth to establish medical schools was Benjamin Waterhouse, the physician, who with John Warren (b. 1753), made possible a medical school in connection with Harvard, in 1782. He also was the first to introduce Jennerian vaccination into this country, which he did in 1800. In all the early efforts to establish medical instruction in this country, the medical aspect of the healing art looms large.

The son of Nathan Smith, Nathan R. Smith, in 1825 published his "Physiological Essay on Digestion," which antedated much that was subsequently discovered. My copy from my grandfather's library bears upon its title page this sentence: "It is no small part of science to be well acquainted with its real boundaries; but it is necessary also to know what it is which truly exists within these boundaries, and what it is which is only fabled to exist." A little later than this time we recall William Beaumont (b. 1784), pioneer physiologist of this country, whose experiments and observations on the "Gastric Juice and Physiology of Digestion," Plattsburg, 1833, were epoch making. Curiously enough, the place of his observations upon Alexis St. Martin was the battlefield of 1814, a portion of which is now occupied by the Military Training Camp, with which you are all familiar.

Passing by many contemporary lesser lights, we come to another epoch-making medical advance. While we may speak of the work of Crawford W. Long and his rival claimants to priority, Jackson, Wells and Marcy, this fact is firmly established: It was William T. G. Morton (b. 1819) who first publicly demonstrated that by

the inhalation of ether unconsciousness sufficiently profound to permit of surgical interference could be produced by medical means. This was on October 16, 1846; the place was the Massachusetts General Hospital, and there are those present in this room who have heard the narration of that event from the lips of those present at the demonstration. It was also another graduate of Harvard, Oliver Wendell Holmes, in his early days a physician, but better known as an author of delightful fiction, both prose and poetry, and a teacher of anatomy, who coined the word "anesthesia," by which this priceless boon to humanity is known throughout the whole world.

Medicine has made modern surgery possible, and to it credit must be given for the wonderful surgical work that is being done today. Parenthetically it might be remarked that anesthesia has also permitted some very mediocre surgery—thus not every great blessing is entirely unalloyed.

Fundamental, also, to the present value of surgery is antisepsis, which has been developed as purely a medical problem, and which has led to asepsis as an ideal of more or less complete realization, although the present European conflict which is now raging has demonstrated that chemical antisepsis is still of great importance.

An epoch-making book of a later date was "Nature in Disease," by Jacob Bigelow (b. 1787), a Harvard professor; my copy, the second edition, bears the date of 1859, although the first was published in 1854. His views on self-limited diseases directed rigid analysis of the value of therapeutic measures. In his dedication of it to Robley Dunglison (b. 1798), the medical lexicographer and another of our medical Nestors, we find: "I am sure that you will unite with me in admitting that the experience of a long professional life is the best corrective of the exaggerated estimate which we are liable to form, or imbibe, in our earlier years, as to the power of medication to control disease." Dunglison also occupied a settee at the University of Maryland, for he was professor of materia medica, therapeutics, hygiene and medical jurisprudence, and his writings comprised systematic treatises upon "Physiology," "Hygiene," "Therapeutics," "Practice" and "Materia Medica."

W. W. Gerhard (b. 1809), of Philadelphia, must claim our attention for a moment, for he was the "first man to distinguish clearly the difference between typhus and typhoid fevers."

Of the more recent developments in medical science due to Amer-

ican medicine we need only to allude to our antityphoid vaccine, the most efficient of any country, to our work on uncinariasis, yellow-fever, pellagra and malaria, to our work on sanitation in tropical and subtropical countries, which has given such brilliant results, the names of those who have made medical history are upon our lips, some are yet living—others, alas, have fallen, martyrs to medical science.

The greatest triumphs over diseases, and even death, achieved during the last half century have been medical rather than surgical. They have been the discovery of the *causa causans* of disease, and the separation of the infections, due to bacteria, or protozoa or other organisms of the lower zoölogical orders, from the inflammations and degenerations. The direct result of our knowledge of etiology has resulted in the preventing of the incidence of disease on the one hand, by intelligent hygiene, and by extensions of the theory of Jennerian vaccination to other diseases, notably diphtheria, tetanus and enteric fever. And a further direct result has been the ability to cure such infections during brief periods, as has been particularly demonstrated in diphtheria, malaria and syphilis, and not only this, but as well, by serological methods, to demonstrate that the cure is absolute and permanent. In others, as acute rheumatic polyarthritis, we have found methods to markedly shorten its duration, directly alleviate suffering, and prevent frequent complications.

Among the constitutional diseases absolute prevention and relative cure has been brought about in some, for example, in scorbutus, diabetes and gout, with a minimizing of suffering in some and averting a fatal issue in others. In diseases of the circulatory system medicine has made startling advances in drug therapy and physical procedures, so that no longer are the problems approached with other than confident expectation of benefit and relative cure so long as degenerations can be checked in their course and structural changes have not extended beyond the possibility of functional recovery. The same may be said of the diseases of the respiratory, digestive and urinary systems. Among the great triumphs of recent medicine may be cited the accurate and productive studies upon the blood, and work upon the functions of the ductless glands, the results of which have been far reaching and of inestimable value, and whose importance in health and disease cannot be overestimated. I need not remind you that these problems are purely the problems of internal medicine, and their solu-

tion depends solely upon the internist. In fine, the most important developments in the healing art, important not only in the larger number of diseases and of major importance, but as well in the larger number of individuals afflicted, has been in the domain of internal medicine. And, furthermore, the greatest progress in the immediate future must of necessity be in this very field.

The record of the distinguished physicians, our medical ancestors, is far too long to be adequately presented in a ponderous tome, let alone in an address. They were giants in those days, of thorough mental training and discipline, of accurate and painstaking observation, of rigid logical analysis and productive clinical deductions. They have contributed in large measure to the advance of medical science and therapeutic art. We are the legatees of these physicians of a magnificent medical past, and as internists we are the trustees of the glorious internal medicine of the future, whose soundness in scientific basis, whose development in the alleviation of suffering and the prevention and cure of disease, and whose value to suffering humanity only the seer must venture to predict. This is the function of the Congress on Internal Medicine; to view with reverence the foundations laid down, broad and deep by the physicians, our medical ancestors, and as internists to raise upon them a useful structure for the healing of the nations.

The Congress on Internal Medicine has for its *raison d'être* (1) to define its domain, (2) to procure recognition of the designation "internists," (3) to promote solidarity of the interest and achievement among them and (4), finally and most important, to advance the science of biological medicine, of which we are the exponents: (a) by the selection of experts who shall report the results of their investigations of important problems and of intensive clinical study and experience, (b) by extending the sphere of influence of the constructive workers in internal medicine through publication of their conclusions, (c) by authoritatively instructing the public in regard to the great problems of health through the official departments and services now organized, and thus render them more efficient.

I do not approach this constructive work of building up the American Congress on Internal Medicine with any misgivings as to the result, even when one considers the ambitious programme which is outlined.

We believe that the time has come when the internists shall be united for scientific advancement, and for the benefit of suffering

humanity, and that this organization shall be controlled by those who have been instrumental in developing internal medicine by modern scientific methods, and that this does not meet a temporary need alone, but its existence and importance will reach far into the future. Of its permanent success I have not the slightest misgivings.

The American College of Physicians, through its council, admits to its fellowship, by election, those recommended by the council of the American Congress on Internal Medicine from among its members. The membership in the college is restricted to those whose practice is generally in the field of internal medicine or especially in the recognized departments of the same. Its obligations are those of a gentleman and a member of a learned profession. It has been said that the American College of Physicians creates an aristocracy among the internists. The observer has discerned the purpose of the founders of the congress and of the college. He forgets that the graduate who has earned the bachelor of arts degree has become a member of the aristocracy of letters created centuries ago. He also forgets that the master of arts degree, won after study and examinations, admits the bachelor of arts to a smaller group in that aristocracy of letters. These are honors which mark attainment of the individual in his progress toward appreciation of the higher relationships of life.

The degree which represented the completion of medical instruction and the satisfying of tests of knowledge in the earliest days of our medical schools was that of bachelor of medicine, as it is today in some other countries. There is *a priori,* no reason why a bachelor's degree should not mark fittingly the termination of undergraduate study in medicine, as it does even now in the other learned professions of law and theology. However, in 1771, six years after its foundation, the University of Pennsylvania returned for the degree of doctor of medicine four men who had been graduated as bachelors of medicine in 1768. Reference to the catalogue of graduates of Harvard University shows that the bachelor's degree only was granted from 1788 until 1810, inclusive. With the granting of the doctorate of medicine, which now became the general practice, a higher degree in medicine became no longer possible. The degree of doctor of science has been bestowed, in recent years, upon doctors of medicine who have achieved eminence, although the degree itself is not distinctive. However, medicine is a branch of physical science, and something

more, even if Bacon characterized it as the conjectural. But Bacon died in 1626, so, presumably, he should be pardoned for his unfortunate designation. So it has come about that distinction has been sought in degrees properly pertaining to the other learned professions, notably the degrees of doctor of laws and doctor of civil law, although so far as I know the degree of doctor of divinity or doctor of sacred theology has not been granted for distinction in medicine *per se*. Fellowship in the American College of Physicians has been safeguarded, so far as human foresight can go, and it is intended to be reserved for doctors of medicine who have achieved eminence in the field of internal medicine as practitioners and consultants, as investigators and scientists, and as authors and teachers. It is intended that fellowship in the American College of Physicians shall mean that its possessor has attained eminence in, and is an authority upon, internal medicine as a whole, or upon some of its recognized subdivisions. To define our meaning: "No one has reached a position of conceded eminence in his profession unless it is made to appear that he is deeply and broadly educated, that he has made some substantial contribution to the literature of the medical profession, and that he has been entirely related to some phase of medical practice for a sufficient time to cause him to be widely recognized by intelligent members of the medical profession, as well as by a considerable number of people who have occasion to be interested in the services which that profession renders the people." The phase which concerns the college is internal medicine. "Authority in the medical profession is not acquired through a medical education that is only ordinary and a practice that is merely usual; eminence in the profession can be acquired only through the assiduous prosecution of medical practice for a considerable time, and through some special work, that has laid the profession under some obligation to the practitioner." Eminence and authority, as used in this connection, must be given a substantial and significant meaning.

The schools of medicine by their own action created an aristocracy in medicine as distinguished from law and theology; it has now become necessary for the internists to select from among their own number those whom they deem deserving of additional recognition. If this, with less reason, has been found necessary for the surgeons, of by no means distinguished scientific heredity, how much the more imperative is it for the internists that we shall recognize in a substantial manner those who have accomplished

much in the upbuilding and the imparting of knowledge in the field of internal medicine!

THE CHAIRMAN (DR. BARTLEY): Gentlemen, it is unusual to refer the President's address to a committee, unless it contains recommendations. This address will probably be published and will be accepted as an authoritative statement of the objects and aims of this organization.

I have not consulted the President, but I feel sure that he will be glad to hear any expressions of opinion, pro or con, with respect to the definitions and the grounds which he has taken in his presidential address. Is there any one who feels that the definitions or statements of the objects of this organization should be in any way modified from the statements given by the President? The address, although it has not been completely submitted to the Council, in the main received the approval of the Council.

DR. L. F. BISHOP, OF NEW YORK: I rise simply to commend the magnificent way in which Dr. Wilcox has put this matter before us.

DR. JOHN C. HEMMETER, OF BALTIMORE: It is unusual to discuss a presidential address, but it is also unusual that the first address at a medical meeting, at its birth, should go by without any comment of the members. I would move, as the expression of the entire body assembled—if there is no criticism—that they approve of the ideas and definitions in the address by a rising vote. Personally, I wish to express my admiration of its lofty ideals and its very high scholarship, and the keen prophecy by which it sees the time maturing when the internists shall group together and stand shoulder to shoulder. I move that the meeting by a rising vote express its approval of the definitions and ideals of the address.

DR. T. E. SATTERTHWAITE, OF NEW YORK, and DR. ALLISON HODGES, OF RICHMOND, VA., seconded the motion, which was carried.

DR. CHARLES E. DE M. SAJOUS, OF PHILADELPHIA: I think that as a representative of the City of Brotherly Love here I could hardly do better than to express on the part of the physicians of Philadelphia their appreciation of the efforts that are being made now in this very connection. I think that Philadelphia has contributed its

share in the line of internists, and of the beginners, as our President has well said; and I am sure that their shades will welcome this great step which is at present so greatly needed. It seems to me, also, that the occasion is a very fortunate one, as far as we are concerned, though on a very unfortunate foundation, in the sense that this war will prevent our European colleagues from doing within the next few hours such work as they have been doing. I think this is a great opportunity for the United States to assert its own worth, its own power, and I believe this Society will do a great deal in that direction.

Dr. W. B. Stewart, of Atlantic City, N. J.: It certainly is a great pleasure to hear this subject presented by a past master of internal medicine, one who is so well known to all of us, and one to whom we look for authoritative statement. I feel that the expressions made by Dr. Wilcox to-day, defining the standards of the internist, and also the qualifications for membership in this Congress, as well as in the College of Physicians, are well made; and I am sure I can so speak for those members of the State Medical Society of New Jersey who represent internal medicine. The time has come when the internist needs to stand out separate and distinct from the mixed surgeon or the surgeon alone.

Dr. Briggs, of Boston, Mass.: I think there are many physicians in Boston who will be glad to know that Dr. Wilcox recognizes Dr. Morton as the discoverer of ether. The question as to who was the discoverer of ether has been before the medical societies for a great many years, as you probably know, and the statue to Anesthesia in the Public Garden in Boston still remains without a name attached to it.

Dr. W. H. Mercur, of Pittsburgh, Pa.: I am glad to see that the Pittsburgh internists are represented here by five members, which ought to be, I think, a good asurance that the internists of Pittsburgh appreciate the value of this movement. Personally I am sure that the other Pittsburghers who are here will share with me in the view which I take of the masterly character of the address, and particularly of the foresight which actuated its writing.

Dr. Roussell, of Philadelphia: I think it is quite apparent to us all that there is a considerable difference between an internist

in the strict sense of the word and a general practitioner. More than that, I cannot feel that the situation is really complimentary to the American medical profession. I think we are rather late in the formation of this particular society. This specialty is distinctly recognized in France, in Germany, and indeed, throughout Europe, and I know of at least one French society that is constituted on the lines that are here indicated. I think that the time has come and that everything is most propitious for the formation of this particular society.

Dr. Robert H. Babcock, of Chicago: I wish personally to endorse the sentiments expressed in our President's address, and I am sure that in so doing I express also the hearty endorsement of the men who come from Chicago, and who feel they have been honored by being chosen members of this Congress.

Dr. Jacob Diner, of New York: There is no question in my mind that every one here enjoyed and appreciated the address of Dr. Wilcox. There is one regret in my mind, and that is that more of the internists are not here to listen to that admirable address. The young men who are entering medicine are always deeply impressed with the spectacular branch of medicine known as surgery. Internal medicine is generally the stepchild of the student. I hope that the Council will see its way clear to have a copy of this address sent to every medical school, in charge probably of the professor or supervisor, so that it may be read to the students. No better summary of the history of medicine in such a brief space has ever come to my notice than that presented by Dr. Wilcox, and I hope that the students of medicine will be given an opportunity of listening, even at second hand, to this marvelous and magnificent address.

The President called on the Secretary-General, Dr. Heinrich Stern, to make his report, and in introducing him, pointed out that it was he who was the real founder of the Congress.

Dr. Heinrich Stern: Mr. President, and Fellows of the American Congress on Internal Medicine—It is six years ago that I started to bring this forward, but it is more than fifteen years that I have been thinking of seeing what is now before us. It was hard work, because the American public, that is the physicians, did not even

know what an internist was. A few graduates from German universities had an inkling of it; but the entire science of internal medicine has really only sprung into existence during the last fifteen or twenty years. When I graduated there was not such a thing as internal medicine. Everything was taken along, and we treated a case without diagnosis, mainly, just according to the symptoms, as well as we could. After I had left college a few years, my two professors of surgery became my two assistants in medicine. The men who subscribed their names under my diploma became my assistants in medicine. But what internal medicine at that time was I had to develop myself, as far as I was concerned. It is true we had some of the older German clinicians; but the German clinicians were quite superficial at that time, too, although they went deeply into the cellular pathology; but cellular pathology, as you well know to-day, is not everything. The laboratory, especially the chemical clinical laboratory, twenty years ago was not even thought of, and the few men who had a little chemical knowledge, just branched out as stomach specialists, because they knew how to test with certain papers for hydrochloric acid and so forth; so it came about that the first internists were really stomach specialists. A general practitioner was almost always a man who thought he knew something about the heart. But when I came into medicine, the heart was hardly ever examined by means of the stethoscope; or if a stethoscope was used it was only a very poor excuse for one; you did not hear much more with the stethoscope than without it. That has all changed in the last twenty, in the last fifteen, years. We tried to do better work, and we know now how to do better work.

Coming down to the present day, that is to this Congress, we were not quite sure whether we should issue cards of invitation for this week,—you must know that we are affiliated now with the American Association for the Advancement of Science, and they meet here in the City of New York at this present time—or whether we should wait until April or May; and we decided, five or six weeks ago, that it had better be now, and we started to send out notices to the profession that the Congress would take place here. We have over three hundred members at this present moment, and a member means a man who has paid his five dollars; not a man who merely makes an application, because we have fifty or a hundred more; but I have received upwards of fifteen hundred letters from men who have declared their intention to join this

Congress but were prevented from doing it this year because the notice came too shortly before the holidays.

The admirable address of Dr. Wilcox told you what we want to do in a scientific way. We want to do even more than he has said. We want to publish a number of scientific journals; whether we shall do that this coming year or the year after, we do not know as yet. It is more than what Dr. Wilcox has outlined that we contemplate doing in a scientific way. But Dr. Wilcox has somewhat neglected to speak upon the financial side, which really ought to interest us. I know we do not come together to discuss finances; but finally all our studies are aimed at producing a better trained man, and the better trained man is the man who has the larger income, as a general rule. Nowadays we may have a certain case; we make the diagnosis, we refer the case to a surgeon, if surgical procedure is necessary; or a surgeon is called in, and the surgeon performs an operation without our knowledge, very often without our consent—very often. But certainly, we are not the participant in the fee. Now, I am not going to talk about division of fees, because that is at once excluded. We do not want to come down to the American College of Surgeons, which was exclusively founded for certain financial purposes and the eradication of certain practices in a financial way. We internists have never as a profession tried to get the better of the patient—never. I do not think there is one real internist—I do not speak of the general practitioner—but I really do not think there is one genuine internist who has stooped down to do his patients. He must not do it, and it is an understood factor. What I would like to say is this: If I am able to make a certain diagnosis—for instance, I say the right kidney is affected, the left kidney is not affected; the condition warrants the removal of the right kidney; I am really the man who bears the responsibility in the case. The surgeon is called in. The surgeon charges $500. The surgeon gets his $500. I get my $25 or $50. It is very nice, but that is not equal compensation. I certainly do not want that patient to pay me more than $250. That is enough. It is all that it is worth. But I want him to pay me $250 and the other man $250. The other man is only my handmaiden. He is nothing more than that. I may order him, or I may not order him; but I ought to have for my diagnosis and for the responsibility which I bear, as much of a financial remuneration as he has.

The first publication, gentlemen, which we ought to bring into

the world, let us call the Internist, if it has to be, and let us advocate in this Journal, which may appear once every second month, or once every third month, how we can elevate our profession. Elevation, in the last instance, can only be brought about by monetary return. If we do not have the monetary return, we cannot buy instruments, we cannot have the proper outfit, we cannot have the books, we cannot go to the centers of learning, of post-graduate study. And that is the point where the surgeon has the advantage. He collects the money. He goes to post-graduate institutions, and he comes back with fresh knowledge, and he can always be abreast of the times. Again, it is really a vicious circle, and you must comprehend it—it is a vicious circle which permits the surgeon to go to the city and to study a little more than his neighbor and makes him also the diagnostician of his little town.

Gentlemen, I wish to provoke a little discussion upon that point, and if the President deems it wise, I am ready to answer all questions.

The President called on the Treasurer, Dr. Augustus Caillé, for his report.

The treasurer submitted his report, which was duly audited, and by unanimous vote was accepted as read.

The President stated that the report of the Treasurer had already been audited by a committee appointed by the Council of the Congress, and ordered it to be placed on file.

The President asked Dr. L. F. Bishop, of New York, to prepare obituary notices of Dr. Peter Brynberg Porter, the late Assistant Secretary of the Congress, and Dr. Frank H. Daniels, the late Treasurer of the Congress.

Dr. Bishop: It is extremely sad at this time to have to present obituaries, and I have not prepared any of the usual statistics with which you are all familiar; but I ask you to take these two men together and consider them in conection with their very earnest backing of everything that pertained to the welfare of the medical profession. Dr. Daniels and Dr. Porter, in the most unselfish way that I have ever witnessed in any department of life, have both given their whole lives to the medical profession, without any ulterior motives. We knew them well; particularly Dr. Porter. For years he was Secretary of some of our great medical societies.

He had a single purpose in promoting the welfare of the medical profession. Dr. Porter was a true Bohemian. Money meant nothing to him whatsoever. If he had enough money for his immediate needs, he never thought about the future in any way. He lived in the simplest manner and devoted himself to the promotion of medical societies. He was Secretary of our County Medical Association and so on. He gave his whole life to the medical profession with no ulterior motive.

Dr. Daniels, in the same way, though more as a practitioner, devoted himself to the profession. And having said that, I cannot say any more, no matter how long I should speak. I think we ought to spread on our minutes an appreciation of what these men did for medicine, and although they can no longer go on with the work, we ought still to give them credit for what they intended to do, because they were among the pioneers in this, what I consider, a great movement.

THE PRESIDENT: The Secretary-General desires the Chair to state that the question of a publication should be considered at this particular time in order to get the views of the Congress upon its expediency or upon its immediate necessity. That is a matter which properly comes before the Council for final action.

Does any one desire to say anything?

DR. J. C. HEMMETER, OF BALTIMORE: One of the most important incentives to the life of an Association is new members. While we will consider that in the Council, the Council is only a very small Committee of this assembly. Therefore I take the privilege to rise in the larger meeting to express the desire to the Fellows, individually and separately, that they will exert their personal influence to increase the membership of this Association at once. You have been inspired by the address and by the ideals that have actuated the foundation of this Association. Now the backbone of an association is large membership, and it can only be gotten by individual work. Printed things sent out to members all over the country have some effect, but not nearly the effect that your personal influence can produce when you return to your separate homes. I hope that these brief remarks will act as an incentive to the members to procure new Fellows all over our country.

Dr. Noble P. Barnes, of Washington, D. C.: I have one suggestion that I would have made before if I had not felt that the time had already been taken up, and that is to get this address of our President into the hands of every practitioner in the United States. The concise, inspiring effort that he has given us this morning, if placed in the hands of the medical profession, will certainly boost the membership of the Congress. I move that the Council consider the advisability of having this address of the President printed and distributed to the medical profession of this country and Canada.

The motion was seconded by Dr. J. C. Hemmeter, of Baltimore, and Dr. C. D. Aaron, of Detroit, and carried.

Dr. Britton D. Evans, of Greystone, N. J.: I think that a rather promiscuous distribution of an address of this character would be a waste of energy, and attended with an expense out of proportion to the results that it might achieve. I would suggest that it be sent to the presidents and secretaries of various medical societies.

Dr. I. M. W. Scott, of Schenectady, N. Y.: I think that this address will be an excellent educational force for the profession.

The President: The only other matter before us is the election of officers for the ensuing year. The mode of procedure which is laid down in the By-Laws is that the Council act as a Nominating Committee, and the names as proposed by the Council will be given to you by the Secretary-General. When they have been given to you, that does not preclude—in fact, it should encourage—nominations from the floor of other names for the different offices.

The following officers for the coming year were nominated by the Council, and were unanimously elected:

President, Dr. Reynold Webb Wilcox of New York.
Vice President, Dr. Elias H. Bartley of Brooklyn.
Secretary-General, Dr. Heinrich Stern of New York.
Treasurer, Dr. Augustus Caillé of New York.

Five members of the Council, of the Class of 1912: Dr. J. Kaufman of New York; Dr. C. H. Jennings of Detroit; Dr. Judson

Daland of Philadelphia; Dr. Francis X. Dercum of Philadelphia, and Dr. H. A. Fairbairn of Brooklyn.

The President anounced that the Secretary-General holds over in office, having been elected for five years, according to the By-Laws.

The Secretary-General announced his appointment of Dr. Joseph H. Byrne of New York as assistant secretary for the ensuing year.

THE DUCTLESS GLANDS IN CARDIO-VASCULAR DISEASES AND DEMENTIA PRECOX

By CHARLES E. de M. SAJOUS
Philadelphia

It is precisely fourteen years ago since I signed the Preface—the portion usually written last—of a work on the internal secretions. Curiously enough, no one seemed to realize at the time, although its title included the suggestive words "Principles of Medicine," the underlying truth that it was sought to convey. This truth, to me at least, appeared to outstrip immeasurably, in importance, that of organotherapy, irrespective of any predominating position this branch of therapeutics might ultimately attain even when the products are become something better than they are now—mere extracts of the factory which produces the secretions and not the secretions themselves. Swale Vincent, however, summarized clearly and succinctly described my aims when he wrote in 1913: "Sajous apparently postulates a relationship between all the ductless glands whose functions dominate most of the bodily activities, normal and pathological, according to this writer."

Time has shown that wherever the field has been sufficiently scrutinized, and some degree of order introduced in the clinical or experimental data collected, there was good ground for the urgent appeal made many years ago. I then compared medicine to "a chain in which the majority of links were of gold and the rest of lead pending the acqusition of sufficient gold to replace the lead," urging that the ductless glands furnished these links. If I am not mistaken, this trend of thought is increasingly proving its soundness, and I would be untrue to my own convictions and perhaps delay progress in the noblest of human endeavors, did I now hesitate to

assert with all the emphasis of which I am capable, that *medical progress which would require fifty years under present conditions, would accrue in probably less than ten years, if the major ductless glands were given due importance in the pathogenesis of all diseases.*

A warning is necessary at the present time, however, to avoid wrecking the ship while it is being launched. One of our most distinguished surgeons, Professor W. S. Halsted, of Johns Hopkins University, a most painstaking and conscientious observer, wrote only last year (1915): "It must be evident to everyone, that there reigns the greatest confusion on the subject of the functions of the glands of internal secretion." The cause of this is not difficult to find. He relied mainly for his knowledge of these functions upon the teachings of physiologists, the normal mentors of this phase of medical thought. We all know the enormous value of their contributions ot our knowledge; indeed, the names of Claude Bernard, Brown-Séquard, Moritz Schiff and other physiologists have been epoch builders, and at the present time their labors are constantly studding our knowledge of the ductless glands with new gifts. Yet, gentlemen, we should not lose sight of the fact that, precious as their labors are to us, their aims are different; they are first of all biological physicists and chemists, we are first of all humanitarians. Indeed, as stated by Dr. L. Faugères Bishop in his work on Arteriosclerosis: "Sick humanity is clamouring for relief and will not wait for the technicians slowly to complete their tasks and, in due time, bear their treasures of knowledge and present them for use. The sick man says, 'Go seize the precious truth and use it now.'" To this I would add: Neither does Death await the laboratory man's results, precious as they are as auxiliaries to our labors.

Our traditions, gentlemen, warrant not only a bold effort to correct a situation which tends to perpetuate the death-dealing trend of many diseases that still defeat all our efforts, but they bid us to proceed with certainty of success. You will probably recall that when that eminent physiologist Professor Pawlow published his work on the digestive glands, he credited physicians with the discovery of their secretory innervation long before this was done by physiologists. "They had even come," he wrote at the time, referring to physicians, "to recognize different morbid conditions of the innervation apparatus. Physiologists, on the other hand, had fruitlessly endeavored *for decades* to arrive at definite results upon the questions. This is a striking, but *by no means isolated instance where the physician gives a more correct verdict concerning physio-*

logical processes than the physiologist himself." Then, to account for this oft' noticed greater insight into physiological truths, he says: "Nor is it indeed strange. The world of pathological phenomena is nothing but an endless series of the most different and unusual combinations of physiological occurrences which never make their appearance in the normal course of life. It is a series of physiological experiments which nature and life institute, often with such interlinking of events *as could never enter into the mind of the present day physiologist,* and which could scarcely be called into existence by means of the technical resources at his command. Clinical observation will consequently always remain *a rich mine of physiological facts.*"

This should not in the least curtail our use of any data physiologists may afford. They should, in fact, be deemed invaluable contributions to our sum of evidence, but what I would urge is that we should cease to depend *totally* upon their labors for the discovery or elucidation of functions which are of paramount importance in the development of our knowledge of disease and therapeutics. All branches of biological science, normal and morbid, are legitimate fields of investigation for elucidative data, but with *clinical medicine as starting point* owing to the vast wealth of material it affords.

The cardio-vascular diseases and dementia precox have been selected to illustrate what the ductless glands might mean to the field of clinical medicine. No question seems to me more worthy of your attention.

The mortality statistics of the recently published Census for 1914, refers to the deaths from organic diseases of the heart as "the largest number classified under any one of the titles of the International List of Causes of Death for that year." It states, furthermore, that deaths from this cause "exceeded the number charged to tuberculosis of the lungs by more than 9,000 and the number assigned to pneumonia (all forms) by nearly 10,000." Turning to what the Census terms the "diseases of the arteries, atheroma, aneurism, etc.," the figures given as annual average for the years 1906 to 1910, are considerably more than twice those for 1901 to 1905. Making all allowances for the many misleading features which such statistics may include, the fact remains that diseases of the cardiovascular system are increasing at a very rapid rate. It might be urged that comparisons with pulmonary tuberculosis and pneumonia, such as those submitted by the Bureau, fail to afford a true idea of the relative values, since both of these diseases may

have shown a decrease of mortality through the improved prophylaxis and therapeutics of recent years. While this criticism is warranted, the mortality of both pulmonary tuberculosis and pneumonia showing a very marked decline, the fact remains that the actual average of both vascular and cardiac diseases of recent years as compared to those of former years likewise show a very marked increase. Facts tend to suggest, therefore, that while we have succeeded in reducing the mortality of tuberculosis and pneumonia, our results in cardiovascular diseases have not been such as to compensate for their rapid increase. Could our present knowledge, deficient as it is, of the functions of the ductless glands, and their rôle in disease, throw any light upon the problems as a whole and suggest remedial measures capable perhaps of raising the standard of our results? If the intimate relationship between the ductless glands and metabolism are recalled, it would appear as if this question could be answered in the affirmative.

ARTERIOSCLEROSIS.

This disease has become one of the most active agents of the fell reaper. The word "disease" is hardly applicable here, however, for if we take into account the many complications it entails, cardiac, renal, cerebral, mental, locomotor, etc., we can well say with Huchard that we are dealing with a *family* of diseases. The complexity of the problem is further increased by the multiplicity of factors which are known to cause arteriosclerosis. Thus, overfeeding accounts for the great majority of cases of arteriosclerosis in the well-to-do; toxemias, including those due to intestinal toxins, gout-breeding purin bases; obstructive renal disorders; continued and excessive physical labor; the violent overstraining of athletes; various infections, notably typhoid fever, rheumatism, tuberculosis, syphilis, malaria, etc.; poisons such as lead, barium, etc.; stimulants, alcohol, tobacco, tea, coffee; worry, anxiety and the general stress of life,—have all been incriminated as causal factors of the disease.

An effort to ascertain the status of the ductless glands in the pathogenesis of the disease, should begin by a full recognition of the pioneer work done by Josué, of Paris, who produced vascular lesions, by injections of adrenalin, resembling at least those of arteriosclerosis, and who created a syndrome for the early recognition of this disease based on the symptomatology of hyperadrenia. We shall see that there is good ground for this attitude in certain cases. But

we will find also that other glands are involved in the genesis of the disease. To make this clear I will divide the morbid process into three types.

Autolytic Type. The pancreas, from my viewpoint, plays one of the leading parts in the process. Besides governing carbohydrate metabolism, it supplies a ferment or ferments which take a direct part in the protein metabolism of the tissue cells, and also in the defensive reactions within these cells, as well as in the phagocytes and in the blood stream.

In the first edition of Internal Secretions (1903-1907), I summarized this feature of the problem in the following words: "The presence of trypsin and other ferments in leucocytes is now recognized as a fundamental feature of phagocytosis. Metchnikoff's cytase is regarded by him, and by Bordet and others, as a trypsin; Kanthack and Hardy also attribute the proteolytic activity of leucocytes to soluble ferments. The more recent writers refer increasingly to the presence in leucocytes of such a ferment." . . . "That trypsin is the bactericidal agent of the intestinal tract has been shown by Charrin and Levaditi, Zaremba and others." After a study of the trophocytes of sponges, laboratory studies of the properties of ferments in lower forms, the migratory powers of leucocytes in higher forms, etc., I concluded that some leucocytes at least, migrated from the intestinal canal to the tissue cells, there to carry on, among other functions, that of katabolism. I also held that in the blood, besides acting as phagocytes, they took part in the defensive process in the plasma when it was invaded by bacteria, toxins, toxic waste products, or other substances harmful to the tissue cells, the katabolic phase of metabolism here serving to break down the pathogenic substances, endogenous or exogenous, precisely as it did wornout components of the tissue cell.

Abderhalden subsequently (1905-1915) reached very similar conclusions. "Everything points," writes this observer, "to the fact that the [tissue] cell has agents at his disposal which render it capable of splitting up into their simplest units all the complicated substances which are brought to it or which it itself builds up." Again, "each separate cell with very few exceptions disposes of the same or similar ferments as those secreted by the digestive glands in the intestinal canal." As to the manner in which the tissue cells are reached by these ferments, he writes, "Many facts accord with the suggestion that the leucocytes play a part in this connection." In keeping with my own views, Abderhalden has termed the digestive

ferment a "defensive ferment," thus bringing, he adds, "the so-called reactions of immunity into close line with processes that are normal and consequently familiar to the cells." Briefly, the same process which prepares foodstuffs for assimilation and breaks them down to eliminable wastes, is used by Nature to convert pathogenic substances likewise into eliminable end-products, thus protecting the organism against their morbid effects. This conception of immunity, while devoid of complexities, enables us to understand clearly many pathological and clinical phenomena that have remained unexplained. In arteriosclerosis, and other conditions to which references shall be made, we witness, among other causative phenomena, *exaggeration of this digestive process, with tissue destruction as result.*

It is not my purpose to inflict upon you a mass of supporting data that have already been published, but I will recall that the presence of digestive ferments in tissue cells has long been recognized. No less an authority than Vaughan, in fact, states (1913) that "the cell which can no longer supply a digestive ferment is already dead, whatever be the kind or amount of pabulum surrounding it." As regards the presence of the digestive ferment in the blood, I may quote Eugene L. Opie's statement that "the ability of the blood to remove injurious material is dependent on the possession of proteolytic enzymes. Peculiar to the polynuclear leucocytes is an enzyme which, like trypsin, exerts its digestive action in an alkaline medium."

Wheeler and Bishop's sensitization theory of arteriosclerosis is also based on the presence of trypsin in the tissue cells, with excess of proteins as main pathogenic agent. Yet, how is this sensitizing process carried on and how are the arterial lesions provoked? We are not dealing here with a sudden anaphylactic reaction, but with, in practically every instance, a very slow and gradual erosion as it were of the vascular walls. How is this morbid process developed? This is where, I believe, the functions of the thyroid and adrenals assert their influence.

While nothing proves that the protein itself activates directly the trypsin zymogen in the cells, much evidence is available to show that it does so indirectly by evoking, in the body at large, a defensive reaction. From my viewpoint, the protein does this *by enhancing the functions of the thyroid and adrenals—beneficially up to a certain limit, harmfully when this limit is exceeded.* In other words, proteins used in excess awaken a reaction having for its purpose to convert the harmful surplus of proteins, both in the cells and in the

blood, into eliminable end-products. As long as the excess is only such as to keep this protective reaction within certain bounds no harm to the tissue cells results, even though the cellular proferment is sensitized; but if, when the protective tide is at its highest level, more proteins are added, the already sensitized cellular proferment becomes activated, and digests the cell itself, starting the destructive process, or autolysis, the precursor of arteriosclerosis.

The sensitizing properties of the thyroparathyroid secretion, which I assimilated to those attributed to opsonin by Sir A. E. Wright has been confirmed by others. Thus Léopold-Lévi and H. de Rothschild, of Paris, write in this connection in the second volume of their *Physiopathology of the Thyroid Gland:* "Sajous has attributed, among the functions of the thyroid body, a rôle to the latter which he assimilates to that of opsonins and to autoantitoxines. More recently, Miss Fassin [at the Bacteriological Institute of Liège], M. Stepanoff, and M. Marbé [at the Pasteur Institute] have confirmed on their side the influence of the thyroid on the blood's asset in alexins and opsonins." For the chemical process involved, which also includes the cellular nucleins, I must refer you to former writings, recalling merely that the high-liver in the earlier stages of arteriosclerosis often presents symptoms of Graves's disease, flushing, sensation of heat, nervous irritability, palpitations, high blood-pressure, etc., and that the thyroid gland or its preparations do not always produce vaso-dilation, as is generally taught. W. E. Waller has also emphasized this fact recently, citing a number of cases of Graves's disease in which, in keeping with some of my own observations, the blood-pressure rose to 170, and in one instance to 250 mm. In the present calamitous war hyperthyroidia has also been found by L. T. Thorne to be accompanied by a rise of blood-pressure. Autopsies of victims of Graves's disease often show, moreover, arterial degeneration presenting the characteristics of arteriosclerosis.

As regards the production of arteriosclerosis by adrenal extractives, so much evidence has been published to that effect that I will only recall a few facts. First observed by Josué, this phenomenon has been witnessed by many other investigators. Some authors have argued that the lesions differed from those of typical arteriosclerosis. The fact is that while in some instances the lesions start in the intima and others in the media, both tend to merge. As regards the influence of the adrenalin upon its genesis, so careful an observer as Biedl writes: "There is no reason to doubt that the changes ob-

served in the vessels of rabbits are the outcome of the action of this substance." Another close observer, Richard M. Pearce, concluded after a study of the labors of Vaquez, Aubertin and Ambard, Rose, Darré, Landau and others, and an examination of 163 adrenals obtained at autopsies of cases of arteriosclerosis, that hyperplasia of the adrenals was an almost constant lesion in arteriosclerosis associated with chronic interstitial nephritis and left-sided hypertrophy, and that it occurred with almost equal frequency in arteriosclerosis with chronic nephritis of the parenchymatous type. He also found it to be a frequent lesion of the arteriosclerosis without nephritis and of nephritis without arteriosclerosis.

Both the thyroid and adrenals being admittedly factors of the problem, by what process does a given substance, say protein in excess, produce the local morbid process?

The cellular ferments are subject to the laws of all ferments, one of which is that their activity is increased by a rise of temperature up to a certain limit. This is precisely what occurs in the present connection. That the thyroid influences oxidation is well shown by the studies of Magnus-Levy, Salomon, Steyrer and others, in which among other conclusive facts, the intake of oxygen in Graves's disease was found to be increased from 50 to 80 per cent. As regards the adrenals, the progressive fall of temperature from normal to 80° F. or even below, which follows their extirpation, the low temperature attending Addison's disease, and the fact that, as stated by Biedl, injections of adrenalin may cause a considerable rise of temperature, point to the influence these organs have on general oxidation—a process which I regard as the most important of their functions. Finally, that the thyroid and adrenals act jointly and are mutually necessary is well shown by the observation of Eppinger, Falta and Rudinger, that adrenalin fails to raise the blood-pressure after the thyroid has been removed. All these facts tend to show that *the increased temperature needed to activate the cellular proferment is supplied mainly through increased functional activity of the thyroid and adrenals.*

Recalling the stimulating influence of overfeeding, particularly of protein wastes on the thyroid and adrenals, and that the excessive activity of these organs so raises the sensitiveness of the cellular trypsin that this ferment tends to digest the very cells which harbor it, through, as we now see, increased oxidation, we are brought to realize how typhoid fever, scarlatina, influenza, rheumatism, tuberculosis, and other febrile infections may initiate the disease.

Alcohol belongs to the same category as a cause since, as we all know, it is by undergoing oxidation in the body that it liberates its energy. The cases due to the excessive use of tobacco probably belong also to this class, Cannon, Aub and Binger having found that injections of nicotine in small amounts in cats caused an increase of adrenal secretion. Gley likewise observed recently that nicotine caused an increase of adrenalin in the blood, while in rabbits Leo Loeb found that the primary lesions caused by nicotine were in the intima. An active defensive reaction such as that occurring in gout, renal insufficiency, syphilis, lead poisoning, etc., is also attended by increased functional activity of the ductless glands. As to the pathological lesions produced, the blood being the active oxidizing agent, the lesions are those of the nodose type, affecting first the *intima,* particularly where the blood is most rich in glandular products, the aorta, where autolysis is most active.

Adrenal Type. This form is that which approaches most nearly Josué's adrenalin type. It differs from the former or autolytic type in that the lesions appear first in the media. As stated by Guthrie McConnell, "the changes which develop do not correspond accurately with those of the ordinary nodose sclerosis, but they are indistinguishable from the changes seen in Moenckeberg's type of medial degeneration." Harlow Brooks and Kaplan reported an interesting case in this connection. To relieve asthma, the patient had been given intramuscularly from 10 to 120 minims daily for over three years. At the autopsy the necrotic foci were found especially in the media. As stated elsewhere, the evidence tends to show that this form is due to excessive constriction of the vasa vasorum, owing to the contracting influence of adrenalin on the smaller or terminal arteries. That the other coats of the vessels may also be involved, however, is suggested by Cowan's observation that while the lesions in the vasa vasorum were sometimes the only visible ones, he had observed cases in which the interference with the vascular supply from the vasal vessels produced medial and intimal necrosis.

To this type probably belong the numerous cases due to excessive physical labor—62 per cent. of 3894 hospital cases studied by Thayer. Abelous and Langlois, have shown that the internal secretion of the adrenals destroyed fatigue products, i.e., toxic wastes generated during muscular activity. This has been confirmed by Mossé and others. The fact that emotions, fear, etc., as shown by Cannon, increase adrenal activity, suggests that cases due to worry and anxiety, also known to play a part in the etiology of the dis-

ease, belong to the adrenal type, though merged in many instances with the autolytic type.

Denutrition Type. A third type imposes itself, however, when we take into account the fact that cases of myxedema frequently show postmortem, advanced arteriosclerosis with typical lesions including calcification. A similar condition has been observed by Bourneville, Marchand, Heyn and others, in hypothyroidia, while premature arteriosclerosis is not uncommon in diabetics, particularly in the advanced stage. The influence of the thyroid apparatus upon oxidation and metabolism, explains this phenomenon—diminished functional activity, obviously defective metabolism and degeneration in the vessel walls. The sclerosis, fibrosis, or calcification found more or less in all forms being a process of local repair, it occurs as well in this degenerative form as it does in the two preceding. In the aged, arteriosclerosis is doubtless due in some instances, to deficient activity of the ductless glands. As is well shown by the studies of Landau, Ecker, Heine, Rolleston and others, the adrenals, for instance, show marked reduction in volume in wealth of vascular channels and of secretory activity, in aged individuals. This applies also to the thyroid.

The fact that hypoactive adrenals do not prevent the development of this denutrition type of arteriosclerosis, suggests that high blood-pressure is not necessarily a feature of the morbid process. Indeed, various observers have brought on the disease by injecting toxics, including adrenalin with agents, amyl nitrite, for instance, which would prevent a rise of blood-pressure, or in doses too minute to affect the latter.

High blood-pressure should be regarded, therefore, more in the light of a very important early symptom, and also as a valuable danger signal in advanced cases, than as a causal factor of the disease.

Having now submitted my conception of the pathogenesis of the disease, its relations to diagnosis and treatment may be briefly outlined.

DIFFERENTIAL DIAGNOSIS AND TREATMENT.

If we would reduce materially the death-rate of arteriosclerosis and its many complications, we should as far as possible learn to establish clearly the symptomatology of the presclerotic stage, i.e., before the bloodvessels have become the seat of lesions, when either excessive adrenal activity, autolysis or arterial denutrition is taking place. The etiology here is, as we have seen, of cardinal impor-

tance. As to the symptoms of fully developed disease, they are virtually similar, being those of arterial degeneration however caused. I will not inflict their enumeration upon you, and refer only to such remedial measures as the pathogenesis described may suggest.

Adrenal Type. Although Josué and others recognize a clearly defined adrenal syndrome, both the prodromic and late signs they describe have seemed to me to occur in the autolytic period as well. Indeed, it is difficult to understand how it can be otherwise, since the power of the adrenal secretion to excite thyroid activity causes both these organs to act synchronously. It has seemed to me, however, that in cases in which sustained exertion, as in laborers, letter-carriers, bicylists, etc., the adrenal factor could be discerned to a certain extent. In such cases, the blood-pressure is apt to be somewhat high—150 mm. or thereabouts—the patient may complain of headache or rather of fullness about the brow and of cramps in the calves of the legs. He may be irritable, or, conversely, exuberant, flushed and buoyant, "feeling like being on the go all the time," as one expressed it. The pulse may be slow and full and the heart beat, though normal, somewhat forcible. Epistaxis, and conditions which the patient defines as nervousness, palpitations, sleeplessness, especially during the early morning hours, a nervous or hacking cough, asthenia or a "wheezing under the breast bone," and often gastric disorders in which hyperchlorhydria and pyrosis are prominent signs. In fact, it is usually for some gastric derangement with constipation, or for muscular pains attributed to rheumatism, that the patient presents himself.

Such men may, in keeping with what is observed in hypernephroma, show great muscular development—sufficient in three cases that I have seen to suggest larval acromegaly—and perspire very freely. They may also show venous engorgement, venous pulse, facial congestion—all symptoms of hyperadrenia—all due to thickening of the arterial coats, especially of the muscular media. Conversely, they may appear pale, complain of cold extremities, and stand cold weather badly. This may be due to constriction of the peripheral arterioles, but in all likelihood to the onset of organic lesions.

Such cases yield readily to measures calculated to reduce the functional activity of the adrenals. A less arduous occupation, abstention from meat, coffee, tea and alcohol, to lower the vascular tension, often suffice. If the vascular tension is high, the condition

of the kidneys should be looked into. As a rule at this time, these organs are found normal though some polyuria be present. Spirit of nitrous ether may then be used in small doses three times daily to reduce the tension if it fails to recede after a few days, and also small doses of sodium bromide and chloral on retiring if the tendency to insomnia persists.

The iodides at this stage are harmful. So are strychnine, digitalis and tonics in general, most of which stimulate the adrenals and aggravate the trouble.

Autolytic Type. This type may either begin with the symptoms described, where the causative poison is one acting slowly, as is the case in the large proportion of patients in whom the disease is due to the excessive use of proteins, alcohol, coffee, etc., or may follow a febrile disease. Here, we are no longer dealing with erethism due merely to exaggerated metabolism, but with the symptoms of the damage the latter is doing or has done to the blood vessels. In the overfed or overworked, as previously stated, we witness the phenomena of stimulation: flushed face, brilliant eyes with perhaps slight precordial pain after an unusual copious meal, or unusual exertion as running, climbing, etc., and general vivacity; but, it is important to note that this stage of primary exuberance corresponds with the febrile period of an infection which may, though relatively very short, do as much damage to the blood vessels as years of overeating, hard labor, etc. The patient, after either of these preliminary periods, long or short, passes into what is now mistaken, and described as such in most text-books, as the early manifestations of arteriosclerosis, but which are in reality those of its second stage. While in the first stage, the vessels are merely congested and more or less thickened or hypertrophied, thus causing the blood-pressure to be more or less high, in this second stage, organic lesions have already compromised their power to contract equably in all parts of the circulatory tree. This may affect one part of the latter more than another, or a morbid process may be awakened in one or more organs, the brain, cord, liver, kidneys, etc., according to the inherited or acquired susceptibility of these structures. It is then that we begin to witness the syndrome which is usually compared to neurasthenia, which is really that of a debilitated circulation: loss of vigor, lassitude, or myasthenia, drowsiness, postural vertigo, faintness, more or less marked visual disturbances, phobias, headaches, dyspnea on exertion, transitory hemianopsia or amaurosis—the whole gamut with which you are all so familiar.

Here again, prophylactic measures, a reduction of proteins—a feature that is harmful in these cases, which a vegetable diet, by supplying alkaline salts, tends to counteract and gradually to eliminate. Although the arteries are already damaged, the process of repair in them is very active, often by insular scleroses so disposed longitudinally as to restore the contractile activity of the vessels to a remarkable degree.

As to drugs, is it rational to give the iodides in cases in which the thyroid secretion laden with iodine in organic combination is taking part in the cellular destruction of the arterial walls? I am glad to note that the experience of Dr. L. Faugères Bishop coincides with mine in this particular. In fact, he refers to patients who were rendered uncomfortable by the abuse of iodides and suggests the possibility of iodism superadded to the symptoms of the disease. This is precisely what happens when the iodides are added to the thyroidine with which the tissues are laden, the thyroid being already overactive. The indications are precisely the opposite: No remedies until the toxic factor, whatever that may be, dietetic, intestinal, bacterial, etc., is eliminated prophylactically. If after a couple of months, the patient does not show the sense of well-being which usually follows well addressed prophylactic measures, and still shows neurasthenia-like symptoms, it is because katabolism and arterial degeneration is still proceeding, owing mainly to hyperplasia of the thyroid. Arsenic in small doses, say 3 minims of Fowler's solution, t.i.d., as shown by Mabille and confirmed by Ewald, Heinrich Stern and others, will then gradually reduce the thyroid erethism. In cases showing actual hyperthyroidia, or larval Graves's disease, ergotin, or the coal tars, are helpful to counteract the vascular supply of both the thyroid and adrenals and thus inhibit their secretory activity. It should be remembered that rest is an important feature wherever exuberant activity of the ductless glands is in order. The iodides and digitalis—the latter an active adrenal stimulant, a fact in which several experimenters have also sustained me—are particularly valuable late, i.e., when the thyroid and adrenals have been in a measure exhausted through the excessive activity that the original cause of the trouble, some toxemia, endogenous or exogenous, has imposed upon them.

Denutrition Type. When in the form just described exhaustion of the adrenals and thyroid has occurred through the excessive activity imposed upon them by toxics, they have reached, from my viewpoint, the condition that prevails in what has been termed the

presenile or senile form of arteriosclerosis. In some persons, even those of frugal habits, this develops early because their ductless glands, through inherited debility, are unable to bear the least exacerbation of activity imposed upon them occasionally by even slight intercurrent disorders, fatigue, emotions, shock, worry, i.e., the wear and tear of existence. Important in this connection also, is the influence of the diseases of children, particularly those attended by fever. Interstitial hemorrhages of both adrenals and thyroid sufficient to reduce considerably their functional efficiency cause lesions which, in after life, leave the organs on the very threshhold of physiological activity. Though able to carry on just the needs of commonplace existence, they prove inadequate to meet the needs of any intercurrent issue. Such people are very early the prey of intercurrent diseases, tuberculosis and pneumonia in particular. They grow old early because, as the wear and tear of life impinges upon their ductless glands, denutrition progresses, including that of the arterial system. Premature involution of the thymus, as I have shown elsewhere, may initiate this denutrition type in the young.

The treatment here is precisely the opposite of that indicated in the foregoing forms. Organotherapy, provided thyroid and adrenal gland and any other organic product used be given in small doses, is of very great value. The iodides, also in small doses, digitalis and strophanthus are all exceedingly helpful. A reduced diet here is not indicated. Besides the thyroid and adrenal preparations already mentioned, some pancreatic product should be added to facilitate intestinal digestion, sustain tissue life and contribute with the other organic products administered to the defensive resources of the organism.

Such are, gentlemen, the relations of the ductless glands to early arteriosclerosis as I interpret them. They seem to me, at least, to be borne out by experimental and clinical evidence, the bulk of which could not be submitted owing to lack of space. So strong is this evidence in the aggregate that it seems to me possible to *conclude that arteriosclerosis is the result of excessive or deficient activity of certain ductless glands, the thyroid and adrenals in particular.*

DISEASES OF THE HEART.

The views submitted concerning the vascular system apply to certain organic cardiac disorders quite as well. A brief summary of the relations between the adrenals and thyroid on the one hand, and the heart on the other, will therefore suffice.

Acute dilatation of the heart, such as the heart strain observed in otherwise healthy athletes, and the so-called irritable heart in soldiers, first described by the late J. M. DaCosta, is but an example of adrenal exhaustion, Brown-Séquard, and forty years later, Oliver and Schäfer, having shown that the secretion of the adrenals caused contraction of the heart muscle. This secretion is poured into the inferior vena cava, the blood of which carries it to the right heart. Now it is precisely the right heart which is dilated. That digitalis or strophanthus which, as already stated, stimulate the adrenals, should be indicated seems obvious. Yet is this the best treatment? No; for we are dealing with extreme deficiency of adrenal secretion owing to exhaustion of the adrenals—what might well be termed acute hypoadrenia. Deficiency of fluids being also a result of severe exertion, hypodermoclysis, in small doses, with adrenalin, or a fluid preparation of posterior pituitary, owing to its wealth in adrenal substance, with absolute rest to enable the adrenals to recover their secretory activity, are more rational resources.

Hypertrophy and Degeneration. This overgrowth of cardiac muscular tissue is usually attributed, in arteriosclerosis, to the increased resistance to the blood column imposed by the diseased vessels, the average caliber of which is narrowed when there is an extreme degree of sclerosis of the visceral arteries and larger vessels, according to some authors. Yet, we know that thickening of the vessels may occur without high blood-pressure, in arteriosclerosis, and that, precisely as is the case in the latter disease, prolonged severe exertion, such as that to which blacksmiths, longshoremen, bicyclists, etc., are exposed, brings on hypertrophy of the heart. The fact that this type is known as "primary idiopathic hypertrophy" shows that the nature of its pathogenesis is unknown. In truth, when we analyze such cases with any degree of care, we find that many of them are in that stage of arteriosclerosis in which general erethism prevails, i.e., before the stage of degeneration has occurred. After a time there occurs in the heart not as a result of increased blood-pressure as is now assumed, but as a result of autolysis, what Tyson and Fussell describe as the "arterial sclerosis atheroma and fibroid thickening so constantly seen in valves and heart-walls."

Briefly, the causes being precisely the same, both the type of hypertrophy and subsequent degeneration described are but counterpart of the form of arteriosclerosis I have traced to excessive activity of the thyroid and adrenals. Nor do the treatments differ,

digitalis and its congerers being harmful in the hypertrophic or erethic stage, but beneficial in the degenerative.

This cursory survey of a few cardiovascular diseases illustrates the importance of including the ductless glands in our conception of their pathogenesis and treatment. Indeed, owing to the non-recognition of these organs, I may add, a large proportion of untimely deaths occur in acute diseases of many organs, and particularly the heart, which might be avoided.

DEMENTIA PRECOX.

Just as cardiovascular diseases now stand first among those which cause death prematurely, so does dementia precox stand first as the destroyer of the mind of the young. In a recent paper, Bayard Holmes states that of the 14,000 insane in Illinois, at least 60 per cent. are cases of dementia precox. This probably represents the average throughout the United States. In other words, over one-half of the inmates of our asylums, to say nothing of the many that are not committed, suffer from, or from the complications of, this dread mental disease of adolescence.

Dementia precox is considered in the present connection for two main reasons: *1.* to recall the importance of a gland, the thymus, which, in the pathogenesis of general diseases, has been almost entirely neglected, and, *2.* to inquire from our colleagues who devote their labors to psychiatry, whether, granting that the thymus underlies the development of dementia precox, the general practitioner, who in practically every instance, sees the initial signs of the disease, without recognizing their meaning (owing of course to lack of special training) could not be familiarized with these early symptoms sufficiently to enable him either to send the patient to the psychiatrist before the morbid process is irremediable, or to treat him himself if a psychiatrist is not within reach.

The participation of the thymus in dementia precox was suggested to me by the fact, confirmed by many clinicians, that, as observed in 1858 by Friedlieben, the size and condition of the thymus was an index to the state of nutrition of the body at large. Fourteen years ago I urged, after a careful study of the relations of the thymus to the brain, that it took part in the development of the latter, the deduction submitted at the time being substantially that reached recently, viz., that the function of the thymus was to supply through the agency of its lymphocytes the excess of phosphorus in organic combination which the body, particularly the osseous, ner-

vous and genital systems, including the brain, required during its development and growth, i.e., during infancy, childhood, and adolescence. I will not submit you to the torture of listening to the evidence already published elsewhere, but will merely recall a few salient facts.

Considerable confusion concerning the physiology of the thymus is evident in the literature of the subject even now. There are at least ten theories available as to its functions. The confusion lies in the fact that each author thought his own theory explained the entire rôle of the organ, whereas it failed to do so when submitted to analytical scrutiny. Yet each, with one exception, had merit in the sense that it represented a *bona fide* feature of the problem as a whole. The exception, that is to say, the function which seemed to find no substantial support was the theory which endowed the thymus with an internal secretion. The evidence sustained strongly, however, the view that its lymphocytes carried nucleoproteids, rich of course in phosphorus as are all nucleins, to the organism at large, including the brain and nervous system, for the development of their neurons.

Another feature which delayed progress in ascertaining the functions of the thymus was the non-recognition by many experimenters of the fact that a proper selection of the animals and removal of the thymus almost immediately after birth alone showed its influence on the body growth, the twelve years before puberty in man, being represented in many animals by but a few days. When these and other facts were taken into account, the functions of the thymus as above described seemed to impose themselves.

The wealth of the thymic lymphocytes in nucleins coincides with the all-important influence which the thymus seems to possess in the production of idiocy. At Bicêtre Hospital, according to Morel, 75 per cent. of 408 non-myxedematous idiotic children, ranging from 1 to 5 years old, examined *post mortem* from 1890 to 1903, showed absence of the thymus. At the request of Bourneville, Katz performed autopsies in 61 mentally normal children, varying in age from 1 month to 13 years, who had died of various diseases. In all of these the thymus was present. Conversely, in 28 mentally weak children examined *post mortem* by Bourneville, the thymus was absent. These observations correspond with the results of complete thymectomy in animals. Basch, Klose and Vogt, Morel and others have observed mental disorders in puppies the fifth or sixth month after removal of the organ.

While the thymus thus shows itself capable of supplying nucleins to the organ of mind, dementia precox also shows in many ways some connection with the thymus. There is a marked reduction of the lymphocytes in this disease which the therapeutic use of thymus gland corrects. Deficiency of nucleins is also shown by the excess of purin bases in this disease. Defective metabolism of the bones is shown by the frequent presence of osseous disorders such as retarded growth, rickets, osteomalacia and fragilitas ossium. Finally, therapeutically, Ludlum and Corson-White obtained excellent results in 3 out of 6 cases of dementia precox, the three patients in whom it failed being old and much demented. While these cases are quite insufficient in number to demonstrate the value of thymus gland in the disease, they are at least suggestive when considered with the other data submitted.

The familiar functional relationship between the various ductless glands suggests that asthenic disorders of the latter should show some mental kinship with dementia precox. The English Myxedema Committee, after an extensive investigation, found that nearly one-half of the patients suffering from myxedema also showed mental disorders. The types most frequently observed were melancholia with delusions and hallucinations, and due, as I suggested elsewhere, to lowered metabolism occurring as a result of the deficient thyroid activity, acute or chronic mania and dementia due, from my viewpoint, to the accumulation in the tissues, including the brain, of intermediate products of metabolism which a normal supply of thyroid secretion would, in conjunction with other internal secretions, have converted into eliminable products. Bernstein found the stigmata of myxedema in practically all cases of dementia precox.

The mental symptoms of Addison's disease also showing considerable kinship with those of myxedema, we are brought to realize that thymic deficiency entails more or less deficiency of the other ductless glands and that we find in the stigmata of these various organs, clues to a possible underlying cause of dementia precox which may so far have been overlooked.

In discussing the relationship between the diseases of the ductless glands and cardiovascular diseases I could speak from the standpoint of clinical experience, but dementia precox being out of my line, I can only bid for light, hoping that the following stigmata of insufficiency of the three main ductless glands apparently concerned in the morbid process may prove of some service. Indeed, in this

disease as in arteriosclerosis, the great desideratum appears to be recognition of the initial symptoms, so as to make it possible perhaps to thwart its progress. The stigmata referred to, reduced to their simplest expression, are briefly as follows:

Stigmata of Thymus Deficiency. 1. Deficient development of the osseous system and of the epiphyses, and deformities suggesting rickets or osteomalacia, due to inadequate assimilation of calcium owing to the deficiency of thymic nucleins which take part in the building up of calcium phosphate; undersized stature.

2. Deficient mental development due to the insufficient production of thymic nucleins to supply the neurons of the central nervous system during its development.

3. A low relative lymphocyte count due to the inadequate formation of these cells by the thymus.

Stigmata of Thyroid Deficiency. 1. Subnormal temperature, cold extremities due to deefctive oxidation and metabolism, the thyroid collaborating actively with the adrenals and thymus (before puberty only as to the latter gland) in sustaining this process. Tendency to obesity.

2. A doughy dry skin, with at times cervical or axillary fat pads due to plasmatic infiltration and circulatory torpor; also in very marked cases, scaly skin and dry brittle hair and nails due to deficient nutrition of these structures.

3. Mental torpor or deficiency where true thyroid stigmata are discernible, complete development of the brain requiring perfect coordination of the thyroid, adrenal, and thymic functions.

Stigmata of Adrenal Deficiency. 1. Muscular weakness and emaciation, pallor, deficient hair growth, sensitiveness to cold, subnormal temperature, all due to deficient tissue oxidation and recession of the blood mass into the splanchnic area.

2. Weak heart action and pulse, low blood-pressure, and constipation due to deficient peristalsis, the result in turn of torpor of the intestinal muscular layer.

3. Pigmentation, sometimes limited to bronze areas on the back of the hands, and freckles.

4. Mental torpor, slow intellection or even idiocy where the adrenal deficiency is initiated *in utero*.

In all these abnormalities we must bear in mind the influence of toxics, exogenous and endogenous, which are now known to bear so great an influence on mental diseases. The functions of the ductless glands including that of converting poisons into eliminable

wastes, their insufficiency entails an accumulation of these poisons, or of intermediate wastes—which are also toxic—and, therefore, the very conditions which promote certain forms of mental aberration. Important also, are the diseases of children in the genesis of dementia precox, since, as we have seen, hemorrhages in the various ductless glands may then occur, which are followed by sclerotic lesions that impair their efficiency. But here, another feature must not be overlooked: the lesions that are sometimes produced in the brain itself, in the course of acute febrile infections.

THE RELATIONSHIP OF THE DUCTLESS GLANDS TO ARTERIAL DISEASES

By JUDSON DALAND
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Dr. Sajous, a pioneer in this field of work, has rendered a signal service in directing attention to the relationship of the ductless glands to arterial disease, and as a universally recognized authority on internal secretions, his opinions demand thoughtful consideration.

His communication is important because of the frequency and seriousness of diseases of the arteries, the alarming increase observed in recent years, the original views advanced as to the causation of arteriosclerosis by irregularities of the function of ductless glands, and the new measures advocated for prevention and treatment.

Arteriosclerosis is erroneously employed as a synonym for disease of the arteries, and leads to confused concepts of pathology. It is a subdivision of diseases of the arteries, and occurs as a *usual* or *occasional* result of *different* pathologic processes due to *different* causes. Atheroma due to age should be sharply differentiated.

Accumulated evidence secured at the bedside and by experimentation clearly proves that overfunctionating adrenals or thyroids produce arteriosclerosis, more especially if long continued or recurring with sufficient frequency. The exact manner in which sclerosis is produced is open to question, and views of observers differ. The solution of the question is beset by many clinical and experimental difficulties, and is further complicated by the frequent association of multiple causes. Blood vessels vary congenitally.

Some individuals possess unusual resistance to vascular disease, and a few show sclerosis as early as the fifth or seventh year without apparent cause. It is conceivable that these vessel wall changes are not primary and structural, but may be secondary, due to hyperfunctionating ductless glands.

Long continued excessive muscular work causes arteriosclerosis, and although the supply of adrenalin is increased, this increase is a physiologic response to the needs of the musculature, and therefore *overwork* is the *primary* cause of the sclerosis. The big muscles of the blacksmith's right arm are occupational. Long continued excessive cerebral work causes sclerosis, more especially of the cerebral vessels, and here again the ductless glands are called upon for increased secretions, but the *primary* cause is excessive brain work.

The habitual ingestion of several quarts of water daily by a brickmaker caused advanced arteriosclerosis, a *part* of which was due to excessive labor. The transportation by the circulatory apparatus of a weight represented by so large a quantity of water adds greatly to the work of the cardiovascular system. Diabetes is often associated with the ingestion of large volumes of water, and in a similar manner produces arteriosclerosis, a *part* of which, however, is due to the products of altered metabolism, and an over- or under-activity of the thyroid or adrenals. Syphilis causes endarteritis, often obliterative, and aneurisms are common. The spirocheta pallida has been observed in the wall of the artery, and this organism and its toxins are the cause of the endarteritis. Rheumatism is accepted as a cause of arteriosclerosis. Recently evidence has been accumulated proving that rheumatism is in reality a secondary manifestation of a chronic septic focus, and is usually associated with one of the strains of streptococci, which has been observed in the wall of the artery. Whatever rôle the ductless glands play in this disease is secondary, and the toxic substances produced by the streptococci and by katabolism aid in the production of the vascular changes.

Gonorrhea, tuberculosis, pneumonia, and typhoid cause arterial disease, and their specific organisms have been found in the arterial lesion. When tuberculosis, pneumonia, or gonorrhea is associated with mixed infection, arterial disease is more likely to occur. The ductless glands in these diseases play a secondary or associated rôle.

Arteriosclerosis has followed scarlatina, variola, measles, influenza, typhoid and typhus fever. It is possible that the so-called

rheumatism and the communicable diseases already mentioned stimulate the ductless glands, and secondarily produce the autolytic or adrenalin type of arteriosclerosis. On the other hand, it should not be forgotten that toxins made by pathogenic organisms may injure one or more coats of the artery, and so provide favorable conditions for their lodgment and growth.

Conflicting views exist as to the etiologic relationship of tea, coffee, alcohol and tobacco to arterial disease. Although Russians consume large quantities of tea, no effect was observed among the patients in many of the hospitals of Petrograd and Moscow.

Coffee exerts a marked influence over the cardiovascular system and in certain cases apparently causes arteriosclerosis, especially observable in Hungary, where this beverage is consumed in large quantities. Many cases of arteriosclerosis, supposed to be due to coffee, are neurasthenics, and the rôle of the ductless glands may therefore be larger than hitherto supposed.

Tobacco produces a marked influence over the cardiovascular and nervous systems, and when used in great excess, may also cause degeneration of the nerve endings. It is difficult to assign to tobacco its exact percentage of value *etiologically* in the production of arteriosclerosis, because it is almost constantly associated with the other causes of this disease.

A typical example occurred in three brothers, all using tobacco to great excess, leading to the supposition that it was the chief cause of the arteriosclerosis. They were markedly neurotic, living a strenuous business life, and at times indulging in excesses of food and wine. These patients doubtless also suffered from hypothyroidia and hypoadrenia.

The products of decomposition or fermentation of the intestinal contents produce arteriosclerosis, and may also stimulate the ductless glands.

French observers have long maintained this opinion, some believing that paracresol and indol of intestinal origin, due to the decomposition of nitrogenous materials, are able to evoke arterial disease.

All are agreed that gout causes arteriosclerosis. Although excess in food, especially rich in protein, with wine and insufficient exercise, are the chief causes, many attacks occur in the *absence* of these causes, apparently due to exhaustion or disturbances of the nervous system, well explained by Dr. Sajous' belief that katabolism may be induced by *lessening* of the activity of the adrenal center, with consequent diminution of the adreno-oxidase; and he further-

more believes that this explanation is equally true of lead poisoning.

From the foregoing, it is clear that in a number of instances the primary cause of arteriosclerosis may be *assisted* by hypo- or hyperactivity of the thyroid and adrenals.

Arteriosclerosis and hypertension usually accompany kidney disease with renal inefficiency.

The retention of unknown toxic substances in the blood at first causes arterial spasm and later sclerosis, hitherto supposed to be *solely* due to the direct action of these toxic agents upon the vessel walls. It is probable that hyperfunctionating ductless glands assist this process.

Hypertension is a usual secondary manifestation of arteriosclerosis, and also occurs in many other diseases. When marked, it could *cause* or *increase* already existing arteriosclerosis by its physical effect, precisely as has been observed in sclerosis of the pulmonary arteries, with no sclerosis elsewhere, due to emphysema. Hypertension may occur as a sign of pre-sclerosis, or as a danger signal of advanced sclerosis.

With notable uniformity Graves' disease is associated with arterial walls that are degenerated and thickened and with increased blood pressure. It is believed that these changes are due primarily to hyperthyroidia and later to variations in this secretion. Additional unknown factors also probably exist, and there may be associated disease of the thymus.

Recent observations have clearly shown that anxiety, worry, fear, and what is usually understood by the term "strenuous living" cause hyperadrenia, which produces arteriosclerosis. *These causes of arterial disease are chiefly responsible, in the judgment of the writer, for the remarkable increase in arterial disease in recent years.*

Dr. Sajous' classification by types serves a useful purpose, not only by detailing sequentially the mechanism by which internal secretions produce sclerosis of the arteries, but also by stimulating inquiry, observation, and experimentation. In order to emphasize my argument with this aspect of the problem, and to encourage discussion, the essential features of each type are briefly summarized:

An important feature of the autolytic type is the fact that trypsin, pancreatic in origin, is the ferment in the leukocyte which makes it a phagocyte, *able* to destroy bacteria in the intestinal tract, and after *migrating* causes *metabolism* of *proteins,* when in an alkaline medium, and *evokes katabolism* of toxic waste products, toxins

and bacteria. Tissue cells contain zymogen or proferment of trypsin.

Proteins in excess sensitize this proferment, stimulate the thyroid and adrenals and so convert harmful surplusage of proteins in the tissue cells and blood into eliminable end-products. If now more protein be added, the stimulation of the thyroid and adrenals is increased, thereby increasing oxidation and causing fever, which activates the tissue cell proferment causing autolysis and *initiating arteriosclerosis.*

The adrenal type is characterized by hyperadrenia, causing constriction of the vaso vasorum of small or terminal arteries, which in turn causes lesions in the media and later in the other coats.

The denutritional type is characterized by hypothyroidia and hydroadrenia, causing defective oxidation and metabolism, which in turn causes arteriosclerosis, with low blood pressure. These conditions have been observed in myxedema, obesity, and advanced diabetes.

A study of the symptomatology of the three periods in the development of arteriosclerosis is of importance in order to diagnose the participation of the ductless glands in the process. Of the twenty-six signs and symptoms mentioned, almost half are common to many diseases. Hypertension, exaltation, nervousness, insomnia, pyrosis, hyperchlorhydria, venous engorgement, venous pulse, palpitation and congestion of the face, most clinicians would ascribe to disturbances of the nervous and cardiovascular systems, and would *forget* the ductless glands. When all or a part of these symptoms are present and no other obvious explanation exists, they may be interpreted as the result of aberrations in the function of the adreno-thyroid apparatus. Pallor of the face, coldness of the extremities or inability to withstand cold may be *symptomatic* of vasomotor constriction, *adrenal* in origin.

The symptomatology of the autolytic and adrenal period of arteriosclerosis closely simulates that of neurasthenia, and this viewpoint opens a *new* field in the *therapy* of this group, care being taken always *first* to *discover* and *remove* the cause.

It is desirable that a series of carefully observed cases presenting the symptoms of neurasthenia, be studied so as to determine whether organotherapy produces the desired results. A similar study should be made in the denutritional period, where definite results may be expected by alternately using and withholding adrenal, thyroid, or pancreatic extracts, the iodides, strophanthus,

or digitalis. An intensive study of this character would give knowledge as to the frequency and variation of individual symptoms, and conditions under which each appears or disappears; and would eventually establish a *pathognomonic syndrome.* A great need exists for a technic by which the ductless gland apparatus may be accurately tested.

It has long been known that in hyperthyroidia, toxic symptoms are promptly induced by two or three grains of the extract of thyroid, and perhaps similar observations have been made in regard to hyperadrenia. Clinical observations of the effect of other substances should likewise be made, conjoined with a special study of the less characteristic symptoms.

The recognition of the participation of the ductless glands in the production of *symptoms* occurring in arteriosclerosis fundamentally modifies therapeusis and demands the use of old and well-tried remedies from this new point of view, as well as a more intelligent employment of organotherapy.

Practically, the *diagnosis* of the pre-sclerotic stage of arterial disease is *frequently impossible, always* difficult, and *usually* only probable. Therefore when arteriosclerosis is suspected or diagnosed, *prevention* or *arrest* may be accomplished by the prompt *detection* and *removal* of *one* or *more* of the causes of arterial disease, coupling with this an estimate of the status of the ductless glands, in order to give the *maximum* aid to the patient in the *minimum* of time.

The greatness of Dr. Sajous' contribution consists in the principle that aberrations in the functions of the ductless glands, more especially of the thyroid and adrenals, *cause* arteriosclerosis. The acceptance of this principle adds *much* to our resources in the *prevention* and *treatment* of arterial disease, and encourages the expectation of a diminution in the morbidity and mortality of arteriosclerosis.

THE DUCTLESS GLANDS IN DEMENTIA PRAECOX

By FRANCIS X. DERCUM.

Before entering into a consideration of the internal secretions in dementia praecox, it is important first to turn our attention to a number of facts of general but very great significance. Indeed, this is absolutely necessary in order that the changes in the glands of

internal secretion and the possible rôle they play may be viewed in their proper perspective. We are impressed in the beginning with the large proportion of heredity in dementia praecox. In this all observers are agreed. Hereditary factors are variously estimated at from fifty-two per cent. by Schott to ninety per cent. by Zablocka. No doubt the differences in the percentages given by different observers are due to a divergence of view, first as to what should be included under hereditary factors, and secondly as to the affections which should be embraced by the general term dementia praecox. Kraepelin, at one time, found hereditary predisposition to mental diseases in seventy per cent. of his cases, though he thinks that this may possibly have been too high. He states that when the inquiry was limited to the direct heredity, i.e., to the occurrence of mental disease, suicide, or severe brain affections in the parents, it yielded 33.7 per cent., which he again regards as too low. From whatever point of view we approach the subject, however, the facts justify the general conclusion as to the frequency of neuropathic family histories in dementia praecox. Such histories present not only instances of frank mental disease, but also of eccentric or unusual personalities, criminals, prostitutes, tramps, vagabonds and other degenerates. The wide range of the hereditary findings is also a fact of some significance. If the inquiry be limited to the direct transmission of dementia praecox, we find that such transmission is relatively infrequent, as a large number of cases, especially the hebephrenics and catatonics, never reach parenthood. It is otherwise, however, if we include the older, the paranoid cases. Ruedin from studies made of Kraepelin's material comes to the conclusion that dementia praecox is probably transmitted in accordance with the Mendelian law of heredity and appears as a recessive quality. He regards the marked predominance of the collateral and discontinuous inheritance over the direct inheritance, the increase of dementia praecox resulting from inbreeding and the numerical relation of those attacked to those remaining normal, as in favor of this view. The significance of a number of individuals of the same family suffering from dementia praecox cannot be questioned. I have personal knowledge of one family in whom no less than five individuals have suffered from this disease. It is also significant that Ruedin—in keeping with what has been already said—found in the families which he studied, other affections such as eccentric personalities and manic-depressive insanity. He also found that it was not at all infrequent

for manic-depressive parents to produce children with dementia praecox, while the reverse—namely, manic-depressive children from dementia praecox parents—belonged to the rare exceptions. Of equal significance are such facts as the following: Ruedin noted that the late or last-born children of a family suffered more frequently from dementia praecox than the older children, and again, that immediately preceding or following the birth of a praecox patient there was frequently a history of miscarriage, premature birth or still-birth.

Other facts, the meaning of which is unmistakable, are those presented by the physical and psychic stigmata of deviation and arrest. Saiz places the frequency of the physical stigmata at seventy-five per cent. Among the latter are physical feebleness, retardation of growth, a too prolonged juvenile appearance, malformations or peculiarities of the shape of the skull, deep, narrow and irregular palate, persistence of the intermaxillary bone, abnormalities of the ears, fingers or toes, imperfections and anomalies of the teeth and other morphological peculiarities.

It may be correct to accept Ruedin's inferences as to the hereditary transmission of dementia praecox as a recessive quality in accordance with Mendelian law. However, the foregoing facts suggest that in addition, the germ plasm may suffer from impairments that affect its general morphological and biological character and profoundly lower its possibilities of growth and development. Among causes which may thus grossly impair the germ plasm we have reason to believe are infections and intoxications affecting the parent. Pilcz, Klutscheff and others have published suggestive statistics as to the frequency of syphilis in the parents, while Diem, Fuhrmann, Ruedin, Wolfsohn and others have published studies on alcoholism in the parents alike suggestive and significant. That syphilis plays a rôle in a not inconsiderable number of cases is proven by the frequency of the Wassermann reaction in the patients themselves. Bahr, for instance, found it in so large a proportion as 32.1 per cent. Such facts do not mean that the patients are necessarily suffering from a syphilitic disease of the nervous system, but rather that the organism as a whole has been hampered, made deviate and degenerate in its development by the presence of the spirochete and its toxins, i.e., that the development of the organism as a whole—and included in this the development of the glands of internal secretion—has been so inhibited and altered that, at a given point of its life, the organism breaks down by reason of

an abnormal and toxic metabolism. Again, it is not necessary that the Wassermann or other tests should yield a positive result. It suffices if the infection has damaged the germ plasm of the parent, and, in keeping with this is the fact that clinical evidences of inherited syphilis are absent in the great mass of cases. Finally, that alcohol damages the germ plasm of the parent must, I think, be freely conceded and its discussion need not detain us here.

The question whether other poisons and infections also play a rôle in causing damage to the germ plasm cannot be definitely answered; but such action is neither impossible nor improbable. In any event, however, their action must be vastly less important than that of syphilis or alcohol.

It may be possible, let us repeat, that the germ plasm may be laden with a direct tendency to the development of dementia praecox, and which tendency is transmitted as a recessive quality, but that the germ plasm may also suffer gross impairments, the results of syphilis and alcohol and perhaps other infections and intoxications must, I think, be frankly admitted. Further, in keeping with this view is the fact that dementia praecox presents itself not as a specific, a sharply delimited clinical entity, but as a group of mental affections which possess the one common factor of endogenous deterioration.

The above considerations point clearly to the involvement of the organism as a whole. We should remember, too, that the existence of the various evidences of morphological deviation visible to clinical observation also imply that other and perhaps more fundamental deviations are present in the organism throughout. Such an organism must present not only abnormalities of structure, but also abnormalities of function and especially of metabolism. That the internal secretions play a rôle in the general disturbance is extremely probable. Dr. Sajous has pointed out the cogent facts indicating an important rôle played by the thymus gland. In keeping with the view he has presented are not only the facts pointing to a defective nervous development, but also the observations of Barbo and Haberkandl of the occurrence of osteomalacia in dementia praecox. However, I believe that we should be very careful in drawing our conclusions. Various facts point to other structures as well. Thus, that the thyroid gland may present abnormalities is a matter of common knowledge. Occasionally it is enlarged, more frequently, in my own experience, it is small. Thus, in seven of my own autopsies in which the thyroid gland was weighed, five

were little more than half the normal weight, one was one-fourth the normal and only one approximated the normal. Again, out of eight pairs of adrenal glands five were greatly in excess, one decidedly below normal and two about normal. Such facts as these are, of course, impossible of detailed explanation; they merely point to a disturbance of the internal secretions. Changes in the glands of internal secretion were also found by Farrant. By far the most detailed study of the weight of the ductless glands in the insane is that made by Kojima in the pathological laboratory of the Claybury Asylum. As far as can be gathered from his tables, his results are practically in accord with my own, for the cases labeled insanities of adolescence and dementia praecox.

The thymus, pituitary and parathyroid glands studied by Ellis and myself did not reveal changes capable of interpretation, though here and there the findings suggested pathological conditions. Of our thyroid glands three out of the seven showed changes in the colloid material and four regressive changes in the acinar cells. The most constant findings in the adrenal picture was the small amount of fat in the cells of the cortex; possibly this indicated a lessened functional activity. However, that there are other glands which probably play a rôle in dementia praecox, the evidence strongly indicates. Clinically our attention is strongly attracted to the sex-glands. We are confronted by the anomalies of menstruation, or by the delayed and imperfect establishment of puberty, on the one hand, or of sexual precocity on the other. Again, there is the history of sexual excesses, sexual vagaries and perversions. A relation to the sex glands is further indicated by the accentuation of symptoms often observed during a menstrual epoch and by the fact that dementia praecox now and then has its incidence in a pregnancy or in repeated pregnancies or in a miscarriage, as though sex gland exhaustion played a rôle. Various writers, among them Tsisch, Lomer and Kraepelin, have assigned an importance to the sex glands. Lomer, particularly, indicated a disturbance of the internal secretion of the latter, but it remained for Fauser to throw an especially illuminating light on the subject. Fauser, as is doubtless well known to my hearers, found in the serum of dementia praecox cases, defensive ferments against the sex glands and against the cortex. It would appear from Fauser's investigations that in dementia praecox a primary dysfunction of the sex glands leads to the entrance into the blood of unchanged sex gland protein, and that in the subsequent breaking up of this protein, sub-

stances are formed which are injurious to the cortex, and which bring about the destruction, the lysis, of the latter. The substance which enters the circulation is the internal secretion, the hormone of the sex gland, not, of course, the germinal product. The blood of male dementia praecox cases digests testicle only, not ovary; that of female cases, ovary only, not testicle. Fauser's results have been confirmed by a large number of investigators, among them, Roemer, Bundschuh, Kafka, Ahrens, W. Mayer, Neue, J. Fischer, and many others. Only in dementia praecox cases could Fauser demonstrate defensive ferments against the sex glands. In cases in which a digestion of the sex glands was unexpectedly found, and in which a diagnosis had previously been made of manic-depressive insanity or of other functional psychoses, the further clinical course of the cases proved that they were really cases of dementia praecox and that the serologic diagnosis had been the correct one. In a number of less definite cases of dementia praecox in which defensive ferments against the sex glands were found only at times, it seemed as though this dysfunction ran parallel with fluctuations in the clinical course. In some cases, again, in a terminal and stationary condition; that is, in cases in which the pathologic process had run its course, no defensive ferments were found against either the sex glands or cortex. Not infrequently, defensive ferments were also found against the thyroid and against the adrenals. Ludlum, of Philadelphia, has also obtained positive results in the thymus. In the cases which reacted to thymus the patients were small, light of build, and presented morphological features of arrest and other abnormalities. He regards them as cases of underactivity of the thymus. Whatever the future may reveal, there appears to be no escape from the conclusion that in dementia praecox there is a deranged metabolism, an autotoxic state, in which abnormalities of the internal secretions play a leading rôle.

It is very probable, further, that in dementia praecox toxic action is not limited to the cortex. Many of the symptoms suggest the action of toxins upon the sympathetic and autonomic nervous systems as well. How the latter react to poisons, e.g., the various alkaloids, atropin, pilocarpin, morphin, etc., is more or less definitely known. Our knowledge likewise extends to the action of the internal secretions, though here, as a matter of fact, our knowledge is less complete. Much information is, however, in our possession. Adrenalin, for instance, induces contraction of the blood vessels, acceleration of the heart's action, dilatation of the pupils,

drying of the mucous membranes, lessening of the secretion of the salivary glands and lessening of the motility and secretions of the stomach and intestines. Similarly the action of the thyroid and pituitary secretions are attended by phenomena that can only be explained by their action upon the autonomic or sympathetic systems. For instance, how full doses of thyroid preparations accelerate the heart's action, increase the secretion from the skin and of the intestinal tract and increase peristalsis, and how markedly pituitary preparations influence the rate of the heart, blood pressure and other processes is also well known. That some of the phenomena observed in cases of dementia praecox are referable to mere quantitative increase or decrease of the various internal secretions, and that others still are due to perversions of these secretions is extremely probable. That phenomena pointing to the action of toxins on the sympathetic and autonomic nervous systems are present in dementia praecox cannot be denied. There are the phenomena presented by the circulatory apparatus, the digestive tract and such other very special forms of apparatus as the iris. In the recognition of the facts lies the explanation of many of the symptoms. Among the latter are the atonic indigestion, the constipation and the dryness of the digestive tract, the phenomena presented by the circulation, the alterations of cardiac rhythm, the fall of blood pressure, the lividity, dryness, moisture, or other conditions of the body surface, the dilatation or other anomalies of the pupil; and other symptoms as well. The point which should be emphasized is that these phenomena must be referred to a toxic action, an action which expresses itself through the autonomic or sympathetic nervous systems. The last mentioned fact acquires additional significance in our studies in mental disease, when we reflect that it is through this system that the emotions, the affects, mainly find physical expression.

It would appear that in dementia praecox the various glands of internal secretion have suffered in the course of the development of the organism, so that their respective functions are subsequently imperfectly and aberrantly performed. It is not at all unlikely that while a number of glands—perhaps the entire chain—are involved in most cases, certain glands by their action, e.g., the sex glands, may dominate the picture; in others again it is the thymus; in still others it is the system of the pituitary, thyroid and adrenals. In favor of the special rôle played by the thymus is perhaps the fact that cases of dementia praecox frequently betray in childhood the

forerunners of the affection. Kraepelin states that very frequently, especially in the case of male patients, it was brought to light that as children the patients had been markedly quiet, shy, retiring, had formed no friendships, had lived only for themselves. Again, especially in girls, accounts were received of irritability, nervousness, stubbornness and obstinacy. Then, again, a smaller group was noteworthy, mostly boys, in which the children were lazy, disliked work, were unsteady, prone to misdemeanors, held to nothing and finally became tramps and vagabonds. In contrast to these are others, likewise more frequently met with in boys, who as children are characterized by docility, good nature, great conscientiousness and diligence, are unusually good and who hold themselves aloof from all improper conduct. It is not difficult to correlate the reserve and obstinacy with the later appearing symptom of negativism; the oddities and eccentricities with the subsequent symptom of impulsivity, and the docility, on the other hand, with the subsequent symptom of automatism at command. It would appear, indeed, that frequently the character, demeanor and conduct of the child foreshadow the later appearing symptoms of the dementia praecox and that the affection really has its inception in childhood.

It should be added in concluding that it cannot be inferred from Kojimas studies that the changes found in the glands of internal secretion, e.g., the abnormalities in their weights, are characteristic for any form of mental disease. However, it must be remembered that Kojima did not study the thymus.

DISCUSSION:

Dr. Harlow Brooks, of New York: I am going to pick out a single phase of this topic which has been interesting me lately and on which I have been doing a bit of work, and that is the rôle which the ductless glands apparently play, and I believe do play in the picture of collapse which develops so frequently in the infections. A group of cases have formed the basis for this study, and since these cases have come into my service, I have experimentally reproduced the condition in animals, which I consider a very much less important fact than the clinical observation and clinical study. In brief, my deductions are, that in many of the infections, particularly in influenza, in aggresive types of tuberculosis, especialy those which are characterized by a high toxic temperature and many other similar diseases, but notably in those two,—also one may put pneu-

monia in this class,—the collapse which takes place so unexpectedly and so suddenly and oftentimes so fatally, is due, not to what I supposed it to be due in the past, namely a degenerative process in the heart muscle, but a degenerative change in the adrenal tissue. You all know who have worked in the histology of this gland how difficult it is to form a just idea of the changes that have taken place because of the great facility with which infarcts occur, especially in the cytoplasm of the adrenal cell. I have tried to bear that well in mind, but in certain instances there can be no question as to the lesion, and therefore we feel no question whatever as to the clinical signs which appear as a result of this lesion. A very brief exposition of the clinical signs would be a circulatory collapse mostly manifested by a very marked hypotension, and where it occurs in hypotensive cases, it is marked by a fall of pulse pressure rather than a fall in pressure as a whole; that is, a drop in the systolic pressure, while the diastolic pressure remains stationery. Another evidence of circulatory collapse is very great tachycardia or bradycardia.. Those instances in which tachycardia develops we have been taught to think are those in which there is an associated defect in the secretion of the thyroid, and we believe that observation of this apparent effect has substantiated our theory. The mental, the psychic depression, and the changed clinical picture of the case, is another very striking feature of these cases of sudden circulatory collapse which appear in these complications of the infections. We believe that we have relieved these symptoms notably by the artificial administration of the gland which we believe to be at fault. I see one member here present who I know has done a great deal of work in this field—Dr. Diner—and who could speak from direct evidence as to these facts.

Another clinical fact to which I wish to call attention, is that when one substitutes the apparently defective secretion of these glands by the artificial, in these instances of collapse, the action of our longer recognized heart stimulant drugs, such as digitalis, camphor, caffeine and strychina on the heart muscle, is much more evident. For example, in cases in which you have given large doses of digitalis without much effect, if the adrenalin secretion is added, a good effect from the digitalis immediately appears. Such also is true of caffeine and strychnia, I believe, although I think we must recognize now that strychnia is not in itself a true cardiac stimulant; but it is at least a muscle excitant, and as such, when used in connection with nature's method of stimulating the circu-

lation, can certainly produce a much better effect than when used alone.

Dr. Smith Ely Jelliffe, of New York: In casting about for a thought with which I might introduce what I have to say, I picked up a copy of Galen on the "Natural Faculties" just before I went to sleep last night, and my mind lit upon the following phrases. In the introduction I find:

"If Galen is looked on as a crystallization of Greek medicine, then this book may be looked on as a crystallization of Galen. Within its comparatively short compass we meet with instances illustrating, perhaps, most of the sides of this many-sided writer. The natural faculties therefore form an excellent prelude to the study of his larger and more specialized works. What now is this nature or biological principle, upon which Galen, like Hippicrates, bases the whole of his medical teaching, but which, we may add, is constantly overlooked, if it be ever presently apprehended by many physiologists of the present day? By using these terms Galen meant simply that when we deal with a living thing we are dealing primarily with a unity, which while living is not further divisible, and the parts can only be understood and dealt with as being in relation to this principle of unity. Galen was thus led to criticise with considerable severity many of the medical and surgical specialists of his time, when acting on the assumption, implicit if not explicit, that the whole was merely the sum of its parts, and that if in an ailing organism, these parts were treated each in and for itself, the health of the whole organism could in this way be eventually restored. Galen expressed this idea of the unity of the organism by saying that it was governed by phusos or nature, with whose faculties or powers it was the province of physiology to deal, and it was because Hippocrates had a clear sense of this principle that Galen called him master. 'Greatest' say the Moslems, 'is Allah, and Mohammed is his prophet.' Never did Mohammed more zealously maintain the unity of the Godhead than Hippocrates and Galen the unity of the organism."

So that in approaching the subject of dementia precox I wish to emphaisze the unity of the organism. We have to consider all the chemical parts of that organism, but it is not the whole organism, by any maner of means. In fact, it is an incommensurably small part of the organism. I trust that you will pardon me if just for a moment I attempt to throw you into an evolutionary mode of

thinking, to realize how from countless ages of the past, life has been accumulating experience—geologists tell us perhaps for a hundred million years—and little by little in that accumulation of experience life has been constructing structural means by which to manage the energy which is pouring in upon it. Man, we know, is the last word in that series of experiments. He no longer handles the immense amount of energy which is streaming in upon him by purely chemical laws. It was not possible for crystals to handle the new accumulating amount of experience in the past, and therefore crystals developed into a form of super-chemisms or vital reactions which, as we well know, was preserved through the function of colloids. Neither when the recations became concentrated into reflex structures, was the reflex sufficient, even though structurally very good, to handle the accumulated experiences. Millions of years, millions of impending forces were gradually finding an expression in men, and therefore he had to construct something else; and when man arose from lower types, a new type of adapter of energy arose; and that new type of adapter of energy we call the Symbol. So then man represents, now as he is, this transformer of energy. He is not a Leyden jar. He is a transformer. He has more than the ordinary five avenues which our kindergarten teaches about the senses. Comparative histology has taught us that we have twenty-five or twenty-six, and maybe fifty or more, receptors for receiving all of the various types of energy about us, and in the reception of these types we must adapt ourselves to unity of purpose—which is what? Solely not for feeling; solely not for feeling and moving; but for feeling and moving *with our fellow men*. So that through the necessity of the social adaptation, all of the various contrivances which finally became concentrated in the structure of man, were finally adopted and adapted. This is the unity of which I speak. That type of concept which fails to recognize the social purposes of the individual, which fails to recognize the reflex activities of the individual and only looks upon the physicial-chemical reactions of the individual, is never going to explain any disease. If this is so, it does not mean, by any manner of means, that we must turn our back upon these chemical reactions, these vegetative level disturbances which have been called to our attention. There are a great many of them, as we know. They have been called, in dementia precox, the somatic or sensible signs of dementia precox. They are numerous. The blood shows a number of changes—changes in viscosities, changes in hematopoietic

activity, changes in the amount of red cells, changes in the amount of the white cells, changes in the exudative activity of the blood vessels, changes in the volume of liquid, and so forth, all of which have been studies in relation to the vegetative control of the blood vessels in dementia precox. But what is the picture? The picture is the same for the blood, the bones, the blood vessels, the pancreas, the thymus, the gonads, the thyroid, the stomach, the intestines. To every organ we can apply precisely the same reasoning. In other words, an enormous amount of disharmony in the results. There is no harmony in the results of any single series of investigations that have been made. Does that mean they are of no use? Not at all. They are all facts. But it simply means that we have to use a truer series criterita for estimating the value of the facts. The counting of them is one thing. The estimation of their value is another. So that when we are told, as we have been told this afternoon, that there is always increased lymphocytosis in dementia precox, we say that it is not so. And so one finds through at least a thousand different studies—there are at least a thousand different studies on the disordered vegetative mechanisms that are found in dementia precox—this enormous disparity results. What does it all mean? It simply means, so far as I can see, that it only represents a series of results, reactions, not causes. They are results of a number of types of activities on the part of the individual, they are reactions to the social adaptation which comes through his psychological processes. Now that does not mean, by any manner of means, that dementia precox is a purely psyschological disorder, any more than it means that it is a purely vegetative nervous disorder. It is a disorder of the individual as a whole, simply directed towards his adaptation in his social activities; and that, therefore, involves his symbolic values, his reflex values and his hormone values.

It seems to me that we stand to-day on the threshold of an enormous opportunity, that enormous opportunity that Dr. Dercum just mentioned in his paper, and that connexus that has just commenced to be established between actual physiological experiment and the result of the action of ideas upon the body: Dr. Dercum has called it emotional reactions, but I have preferred to call it the symbolic reactions of accumulations of psychical values that the individual has been building up, and which are to express himself in his relations to his fellow-men. When Cannon's cat, in the laboratory, is brought face to face with an infuriated dog, the symbol, a series

of reactions, takes place—the ercetion of the hair, the arching of the back, the raising of the upper lip, and finally a series of chemisms, increased adrenalin content, increased coagulability of the blood, etc. We now have established for the first time the physiological relationships between the psyche, the symbol, and the unconscious accumulation of energy which expresses itself through the vegetative nervous system, of which the endocrinous glands are only a part, because the endocrinous glands are under the control of this vegetative nervous system, and the vegetative nervous system is not under the control of the endocrinous glands. In other words, life began by chemical interrelationships millions of years ago, and because these chemical interrelationships were not sufficient to handle the problems, living matter constructed nervous interrelationships in order that quick exchange might take place between all of the parts of the body. The vegetative nervous system, serving as a medium of this interrelationship, acts upon all the constituents of the body and brings them to serve its purposes. Thus we can see the endocrinous glands try to make the body subserve its purposes. An endocrinous gland disturbance, for instance, is never going to explain why a patient of mine says: "I go up three steps and stop." She is speaking of going up-stairs, and she says in response to my inquiry, "Why do you do that?" "Because if I don't, I cannot have a movement of the bowels." Now what does that mean? Of course we know that it means something symbolically. It is something in the mind of the individual that is influencing her conduct. Yes, she has constipation, too; I grant you that. But the constipation which is due to the disturbance of her endocrinous glands is really the result of the series of ideas in her adaptations, and if one attempts symbolically to find out what she means by going up three steps and what she means by not having a movement of the bowels, what she says appears not nonsensical at all; because what she really says, behind the symbol, is that "without sexual intercourse I cannot have a baby." Well, that is perfectly good sense. "Three steps up-stairs" is sexual intercourse. Movement of the bowels to her is "having a baby." We know that her perverted chemisms are not going to give her that idea; but we certainly get help from the hypothesis that that idea could produce her perverted chemisms. The cat's perverted chemisms did not bring the dog in front of her, but the picture of the dog did bring changes in the cat's vegetative and endocrinous gland.

If, therefore, we are, as physicians, interested in adhering to the

Hippocratic idea of the individual, when we consider the subject of so serious a malady as dementia precox, we must consider the human organism in a three-fold relation.

Man is not a metabolic apparatus only, accurately adjusted to a marvelous efficiency, through the intricate mechanistic adjustments of the vegetative nervous system, nor is he solely a group of complex sensori-motor reflexes, making him a feeling, moving animal—seeking pleasure and avoiding pain through such reflexes alone; nor yet is he exclusively a psychological machine, which, by means of a masterly symbolic control over the vast hordes of realities about him has made him and raised him above the lower animals. Man is all three, and not only the problem of dementia precox, but that of any disease of the human being is to be solved by seeing him as a corelation of all these types of activities.

Dr. Robert H. Babcock, of Chicago: My ideas are hardly yet crystallized into very definite notions concerning these subjects that have been discussed this afternoon. I will say, however, that my experience, my clinical observation, is certainly convincing me of the very important influence of the two ductless glands, the adrenals, and the thyroid, in the production of cardio-vascular disease. It seems to me that we cannot differentiate the factors at work. In other words, we have to consider that a good many factors are at work in their influence upon, for instance, the adrenals, in the production of arterial hypertension, and I only speak of two. I am becoming quite an ardent adherent of Crile's theory of the influence of infections upon the kinetic system, and in particular the influence of infections, whether focal or general, upon the adrenals. It has seemed to me that in a number of instances I have been able to satisfy myself certainly that infections, frequently focal infections, were very important factors in the production of arterial hypertension. I am going to speak of just one other thing. Dr. Sajous has spoken of the influence of protein, the excessive consumption of protein in the production of arterial disease. There is one phase of that which it seems to me is worthy of consideration; namely, that one of the amino acids produced in the digestion of proteins; namely, tyrosin, when acted upon by the bacillus, aminophylus intestinalis is changed into tyramin. Tyramin increases the blood pressure (being in this regard 1/14 as powerful as adrenalin); and we should not ignore the possible influence of this product, this toxic amin, in those cases in which we find our patients have been

undue feeders, and especially undue consumers of protein out of proportion to the amount of exercise they take.

Dr. Ernest Zueblin, of Cincinnati: As to arteriosclerosis and the consequences affecting the vascular system, we are all much interested in the new investigations promising to show that the internal secretions, that the ductless glands, must have a certain share in its etiology. It is a very fine problem to discuss and I would only refer to a few practical observations. In former years we were always taught that arteriosclerosis is always connected with hypertension; that sooner or later we must encounter a hardening of the vessels; that sooner or later we must be confronted with a hypertension; but it seems also that the view is expressed and is emphasized that hypertension can be found and precede the disease. Among my patients I find frequently a hypertension which may be persistent for years before we encounter any further vascular disturbance. It seems to me that in investigating the intestinal functions, we find frequently an aberration in the metabolism, faulty utlization of the proteids; we frequently find added to this trouble, an indicanuria, with symptoms of toxemia, with autointoxication. By paying attention to the input of proteids and their metabolism and utilization, I think we can help to a great extent the circulation by preventing intestinal stasis and venous congestion, and so keeping up a normal circulatory efficiency. If we remember that the heart depending entirely upon itself sooner or later will fail, we must be impressed by the utility of helping its function by prophylactic, medicinal and dietary means. It seems to me, according to my experience with women patients, that at certain ages cardiac dilatation takes place; that at the period of their menopause their heart is apt to present disturbances as regards regularity and as regards size; and in those cases pituitary gland medication seems to give rapid and satisfactory results. The idea has been suggested that perhaps in the progress of age we can have a subfunctioning of that gland. Could it not be possible that the pituitary gland during life plays an important rôle in the maintenance of a normal circulation? Of course, discussion as to the relation of pituitary substances as cardiovascular stimulants cannot be closed, but practical results obtained by their use suggest further investigation. It seems to me that probably no organ is absolutely independent of the function of the endocrinous glands, and it gives me pleasure to see this discussion directed toward the relation of the internal secre-

tions to the general circulation, as well as to all the functions of the organs. That means a very interesting, a very promising field for experimental studies aided by clinical experience, through the practitioner in internal medicine.

Dr. Tom Williams, of Washington, D. C.: I think the contributor mentioned a very important principle; namely, that one must look at the whole man. At the same time, I fear that the way in which that was said may lead to misapprehension on the part of many who are not so well acquainted with dementia precox as psychiatrists are; namely, that dementia precox might be interpreted (and there again we shall fall into the error of not looking into the whole man) —as a psychic disorder, in origin, a failure of psychic adaptation because of defect in the psychic regulation. If we interpreted Dr. Jelliffe's remarks in that way—however he means to interpret them —we should fall into error, because there are certain facts to the contrary. First, the familiar experience of every internist who finds failure in the psychic adaptation known as delirium, in the infections and in the intoxications, which is removed when the physical agent which is disturbing the chemical processes is removed. Now we don't know what the disturber of equilibrium in dementia precox is. We don't yet know that it is chemical or vegetative or physical or, as Dr. Dercum says, a condition of reactivity due to Medelian heredity. Even if that is true, it has to be explained. Now how can we reconcile the fact of failure of psychic adaptation with the recovery from that failure by purely physical-chemical measures, such as those quoted by Dr. Sajous when he spoke of Dr. Ludlum's observations; and I might add some observations which Dr. Holmes has made, in which chemical intervention has removed a situation of non-adaptation, which we call dementia precox. Only by thinking of the whole man, thinking of him as a series of links, a series of faculties by which he is able to adapt, then, wherever the break is we may have the failure of adaptation. This may take the form in certain individuals, whether predisposed or through newly arising causation, of what we call dementia precox. In other words, in some failures of chemico-vegetative capacity leading to interference with cerebral metabolism, we may still have dementia precox; but our intervention in that case would be futile if it confines itself to rectification of the symbolic devices, as Dr. Jelliffe called them, of which he gives a very speaking example: for the patient's disturbance of symbolism there is not psychic at

all. It is due to the fact that this material apparatus fails to coordinate in what we call a healthy way and will not do it until we rectify the chemical basis upon which that cerebration depends, just as we do in the case of eruptive fevers or of the chemical intoxications. So we are back again to the whole man, back again to what Dr. Sajous has said, back again to looking not only at the basic, fundamental, anabolic chemistry of the body which is so important in arteriosclerosis, but in looking at the relation of the balance of the endocrine function and the several parts of the metabolism and then considering the pure psychogentic disturbance of the individual. One word in reference to the psychogenetic disturbance. Where we can trace cause and effect between failure of social adaptation and some psychological influence, some idea disturbing the emotions, our experience shows that it can be rectified by psychological means; but our experience also shows that in the condition which we call dementia precox, in spite of the most assiduous attempts by psychological means, with all kinds of skilled assistants, we fail to secure readaptation of the individual. We have to have recourse in that situation to physical agencies and we have the right therefore to infer that dementia precox is a disorder of physical origin, having nothing to do with the psyche proper as regards causation.

Dr. Francis X. Dercum, of Philadelphia: I know of course that in diseased mental states the individual fails in adaptation to the environment; but why does he fail? Is it not because he is ill? What interests me are the questions, why is he ill? What is the nature of his illness? Is he ill because of a defective organization, because of a defective evolution of his glands of internal secretion, because of some inherited disease, because of some obscure disorder of metabolism or perhaps because of some as yet entirely undiscovered pathological condition? Psychological interpretation of symptoms may be interesting, but the first and fundamental fact for the physician to recognize is that the patient is ill. Psychological speculations are certainly of far less value than studies which show the close relation of psychiatry to internal medicine. Indeed the closer psychiatry is brought to internal medicine, the better both for the patient and the psychiatrist. A patient is a patient; he is sick in a material way. It is for us to find out what the matter is with him, why he behaves in this strange disordered manner. He does not do it wilfully; he does it because he is ill physically. This is the

problem it is our business to solve. This problem comes first. Other matters may be interesting and may lead to all sorts of speculations and theories, but never to actual, enduring results.

Dr. Charles E. de M. Sajous, of Philadelphia: Dr. Daland referred to the action of bacteria upon the vessels themselves. Indeed, we are taught generally to look upon the actions of toxins and endotoxins upon the vascular elements themselves. This point is a very important one in connection with the ductless glands. From my viewpoint, I doubt whether we can really credit to the toxins, or to the endotoxins themselves, the morbid processes that we find in the arteries. When the ductless glands are taken into account, many facts tend to show that it is really not the bacillus itself, or its toxin, that causes damage to the vascular endothelium, but the antibodies which, while carrying on their bactericidal function, include in the digestive process this entails, the endocardial and particularly the valvular tissues. Briefly, autolysis of these structures occurs along with bacteriolysis, and valvular lesions are initiated. A similar process affects the vascular elements when these contain bacteria, and the defensive process is very active in digestive power, digestive ferments being potent factors, we have seen, in the defensive process.

Concerning Dr. Dercum's remark as to the synchronism of various ductless glands in the morbid process of dementia precox, I may recall that it is one of the features that I had previously emphasized, and that while I look upon the thymus as the main factor, it is because it is the predominating ductless gland in the morbid process; just as the thyroid predominates in myxedema although other glands are involved. In fact I may recall that besides those of the thymus, I enumerated the stigmata of these various glands in the paper just read.

I was very much interested by the remarks of Dr. Brooks. He will find considerable support in the second volume of *Internal Secretions* for the views advanced.

As regards the remarks of Dr. Jelliffe, I can only concur with the views expressed by Dr. Dercum and Dr. Williams as regards the need of active treatment if the deplorable ravages of dementia precox are at all to be checked.

THE DIAGNOSIS OF DUODENAL ULCER

By JOHN B. DEAVER

The diagnosis of typical duodenal ulcer should not present any difficulty in view of the fact that the symptoms usually appear in a well-defined sequence, so well defined, indeed, that I should not hesitate to diagnose a typical case from a history given by correspondence or over the telephone, and would feel perfectly confident of having my diagnosis confirmed at operation.

The typical case history of duodenal ulcer reveals years, if not a lifetime, of attacks of epigastric discomfort after meals, that is to say, a fulness, often described as a "blown out" feeling, and a gnawing, burning sensation, rather than pain, with acid eructations, coming on from two to six, commonly three to four, hours after meals. This distress or pain, as many patients call it, rarely appears after the morning meal, but comes on with constant regularity after the heavier meals taken at noon or in the evening; the so-called hunger pain at night (about 2 A.M.) being one of the distinguishing features of the complaint. No satisfactory explanation has as yet been forthcoming as to the rationale of these hunger pains. Moynihan attributes them to changes in the muscular activity of the stomach and the duodenum stimulated by changes in the chemical quality of the chyme, especially toward the end of digestion. Food relief or subsidence of pain upon eating or taking an alkali (soda) is another characteristic symptom. The periodicity of these attacks with intervals of complete well-being is emphasized by all authorities. Moynihan claims that they usually occur in winter and are the direct result of "cold." In my experience, and I have no doubt in that of others also, the spring and fall seasons, if any, are the ones generally mentioned.

The patients are usually middle-aged males. In an analysis of the latest series of 53 cases of duodenal ulcer operated on by me at the German Hospital of Philadelphia during the past year (January to December, 1916) there were 47 males, with an average of 41.5 years, the youngest being 21 and the oldest 63 years of age. The average of the 6 females was 36.8 years.

The physical signs consist of more or less tenderness and rigidity in the epigastric and upper right rectus regions. These, however, are of secondary importance, as it is the history mainly, and I may say exclusively, that counts in the diagnosis of the typical case.

Hemorrhage from the bowel or by mouth, as evidenced by tarry stools or by occult blood in the vomitus, is usually noted in about one-third of the cases. It was a feature in about one-seventh of the histories in this series. These patients also show a low hemoglobin percentage, though none of them presented as low a count as fifty per cent., noted by some clinicians.

Vomiting is not considered one of the commoner symptoms of ulcer of the duodenum, but it was mentioned in about one-fourth of our cases.

High acidity, that is, an excess of free hydrochloric acid, generally conceded to be pathognomonic of the disease, was noted in more than half of the cases; subacidity and normal acidity being about equally divided in the remainder.

The motility of the stomach is an important item in the symptom-complex of duodenal ulcer. That its activity is abnormally rapid is shown by the fact that in a good percentage of cases nothing of the test meal or the full meal is recovered in the usual time when the stomach is siphoned after the administration of the meal. This hypermotility of the stomach is also demonstrated by the X-ray and bismuth meal; they are thus of confirmatory rather than contributory value in the diagnosis.

Briefly stated, then, we may say that epigastric distress three or four hours after meals, relieved by eating or by alkalis; high acidity, hyperactivity of the stomach, and, in some instances, vomiting and hemorrhage are indicative of duodenal ulcer, that is, of the typical case. A correct pre-operative diagnosis was made in all but eight of the series of the present year. In one instance stone in the common duct was diagnosed in addition to duodenal ulcer and both conditions were found at operation. They were corrected by choledochostomy and posterior gastroenterostomy, the patient making an uneventful recovery. But the diagnosis is not always such smooth sailing. There is another variety—the atypical —that leads us into troubled waters. This can perhaps best be illustrated by a case taken from the series during the past year.

Male, aged 32 years, gave a history of moderate epigastric pain for one year past, coming on three or four hours after meals. The pain does not radiate; relief is obtained after eating or after vomiting. Of late the pains have increased in severity and have been coming on one-half hour after meals and have been aggravated by eating meat. There is no longer the food relief as at first, vomiting alone now affording relief. For the past six weeks

the epigastric distress has been regularly accompanied by pain in the right loin near the spine, with radiations down to the right iliac fossa. Vomitus of late has occasionally been blood streaked and stools at times tarry. Urine also has sometimes of late been red. The patient complains of frontal headache and loss of weight, having lost fourteen pounds during the last two months, but seems to be gaining at the present time.

Physical examination shows a pale, sallow, anemic adult male. Abdomen: slight upper right rectus rigidity, very active peristalsis, slight tenderness on deep palpation, especially in the right loin near the spinal column and over McBurney's point.

At operation a duodenal ulcer was found welded together with the great omentum, the hepatic flexure and the pancreas. The appendix was bound down with its tip in the subcecal fossa. The appendix was removed; a posterior gastroenterostomy was done; the duodenum was not plicated.

The patient left the hospital in excellent condition without any evidence of gastric disturbance.

These atypical cases more often simulate appendicitis, especially where the appendix is high, than other conditions from which they can with more or less ease be differentiated, such as gastric ulcer, cholelithiasis, cholecystitis, chronic pancreatitis and pancreatic lymphangitis.

Chronic appendicitis frequently presents the same hunger pains as in duodenal ulcer, hyperacidity is not unusual and many cases show the same chronicity as in duodenal ulcer. The main difference between the two is the freedom from discomfort in the duodenal ulcers between the attacks, while in appendicitis the flatulency and discomfort are apt to be constantly present. But these patients with "appendiceal indigestion" usually suffer more pain after certain kinds of food, especially starchy food and red meats. The pain, however, usually is not so severe as in duodenal ulcer and radiates downward. The latter being one of the main points in the differential diagnosis. In appendicitis exercise frequently increases the local discomfort—not so in duodenal ulcer. In fact, the appendix is found diseased in so many cases of duodenal as well as of gastric ulcer, that these latter may be considered secondary conditions; that is to say, the result of infection from some other organ with the evidence strongly in favor of the appendix as the *corpus delicti.* I, therefore, make it a practice to remove the appendix in practically all cases of gastric and duodenal ulcer.

Some authors claim that it is almost impossible clinically to differentiate between gastric and duodenal ulcer, but it seems to me that there are enough points of variation to enable such a differential diagnosis to be made with some degree of certainty. In distinguishing between the two we may to some extent be guided by the time relation of the ingestion of food and the onset of the symptoms. Although the chain of symptoms of duodenal ulcer is said to be not much affected by the location of the ulcer, it is generally conceded that the longer the interval between the meals taken and the appearance of the pain and the more prompt the food relief, the lower down will the ulcer eventually be found. Therefore, if pain appears soon after eating, in one-half to two hours, and the food relief is not prompt, we may logically expect to find a gastric rather than a duodenal location. Again the radiations of pain, if any, in duodenal ulcer are usually to the right, while in gastric ulcer the pain radiates to the left as a rule. The pain also is apt to be more constant than in duodenal ulcer. Einhorn's duodenal bucket has been found useful in some instances in approximating the location of the ulcer with more or less precision, but I have not introduced it as a routine procedure in my service at the German Hospital of Philadelphia. Vomiting is also more frequently a symptom of gastric ulcer, as is also hemorrhage, the latter usually in the form of hematemesis, while in duodenal ulcer it is more generally melenic.

Cholelithiasis presents rather more difficulty, but care in taking the history will usually enable the experienced clinician to forecast the true state of affairs. The diagnosis is oftentimes uncertain when adhesions exist between the gall-bladder and the stomach and the duodenum, or when the gall-stones have pushed toward the duodenum; hyperacidity being also a symptom of gall-stone disease, adds to the confusion. On the whole, however, cholelithiasis is marked by such severe colicky pain with sudden and unaccountable onset, and almost as sudden and mysterious cessation, that recognition should, as a rule, be easy. Lavage will frequently cut short an attack of biliary colic, but has no influence on the pain of duodenal ulcer. In this connection Moynihan mentions the gastric crises of tabes dorsalis, as a possible source of error in diagnosis.

Chronic cholecystitis very frequently clouds the diagnosis of ulcer, especially of the perforating duodenal ulcer. It presents the same chronicity, though the attacks do not last so long, the pain, hyperacidity and flatulency also present show a certain degree of relationship to food intake, while not infrequently the absence of

typical jaundice in cholecystitis and its presence in duodenal ulcer, as noted in several of our cases, make confusion worse confounded.

Symptoms similar to those of chronic pancreatitis or some pancreatic involvement, such as pancreatic lymphangitis, are not rarely met with in duodenal ulcer. This is not surprising in view of the close relationship existing between the duodenum and the pancreas and the frequent infiltration of ulcer into the pancreas itself and the close intercommunication between the pancreatic and the duodenal lymphatics. For example, loss of weight and strength, a fairly constant clinical feature of chronic pancreatitis, was recorded in one-third of our cases during the past year. The character of the pain in chronic pancreatitis is moderate, as it is in the majority of duodenal ulcer cases, and there is the same epigastric oppression. A valuable distinguishing feature, however, is the absence in the pancreatic disease of any definite relation to eating or drinking, or to the kind of food taken.

Malignant neoplasms of the intestines, in their early stages, sometimes simulate the symptoms of duodenal ulcer, but careful inquiry will usually elicit the fact that the attacks, though presenting the same periodicity as in duodenal ulcer, bear no relation to food, neither in their onset nor in the relief of symptoms. In these atypical cases, however, nothing short of incision and inspection will enable us definitely to determine the nature of the lesion.

Two cases of the present series diagnosed as acute appendicitis both proved to be subacute perforating ulcers which had been closed by plastic exudate. A pre-operative diagnosis of chronic appendicitis in one instance proved correct, but an ulcer of the duodenum was also found.

In four cases a clinical diagnosis of gall-bladder disease was made and in two ulcer of the duodenum was present in addition to the cholecystitis. In one case the diagnosis wavered between carcinoma and ulcer of the duodenum; operation revealed the latter.

In thus giving a cursory summary of the main diagnostic points of ulcer of the duodenum, I may say, I hope, that I speak from a wide experience. During the past six years I have treated by operation four hundred cases of diseases of the stomach and duodenum, of which two hundred were duodenal ulcers. With your permission, I should like to say a few words with regard to the treatment of these ulcers. I know that I risk incurring the displeasure of the internist when I say that he is responsible for a large number of cases of malignant disease of the gastrointestinal tract by

attempting medical treatment of these gastric and duodenal conditions for any prolonged period of time. It would take me too far afield to enlarge upon the likelihood of malignant degeneration of these ulcers, especially those of the stomach. Suffice it to say that the percentage is variously estimated to be from thirty-five (my cases) to seventy per cent. (other authors). Add to this the fact that in our latest series of cases three specimens of duodenal ulcer were returned from the pathological laboratory bearing the legend "incipient malignancy," and you will realize why I make this statement. A serious and more frequent menace presented by duodenal ulcers is perforation and hemorrhage. I find from my statistics that perforation takes place in about fifteen per cent. of the cases and that fully eighty per cent. give a history of previous gastric disturbance. I have had only one death from hemorrhage in these cases. This patient refused operation at the opportune time and died of hemorrhage from the bowel while still in the hospital. At autopsy an ulcer was found on the pancreatic side of the second portion of the duodenum.

With an operative mortality of 3.7 per cent. in the chronic duodenal ulcers and only one death among forty-six perforated cases (thirty-six recent statistics at the German Hospital and ten cases of an earlier series), surely it is, to say the least, unjust to subject these patients to the discomfort and the risk of recurrence and the more serious dangers already alluded to.

We were able to trace about thirty per cent. of the cases of perforated duodenal ulcer cases, all of whom reported well without return of symptoms; the others reported occasionally epigastric distress after eating. One case gave a history of hemorrhage from the stomach due to exertion, this took place three years after operation.

As to the type of operation. Incision and drainage of subdiaphragmatic abscess was found sufficient in one of the perforated ulcer cases, in all the others a posterior gastroenterostomy was performed. In thirteen instances this was the only procedure; in seventeen it was combined with pylorectomy, and in one case in which there was also a gastric ulcer located on the lesser curvature of the stomach necessitating a subtotal gastrectomy. In ten cases the ulcer was invaginated and in five it was excised; plication of the duodenum was done twice. In accordance with our usual procedure, the appendix was removed in all cases, except where it had already been removed at a previous operation. In one other case,

besides plication of the duodenum, the ulcer was invaginated. In the cases complicated with cholecystitis a cholecystectomy was performed in two instances, combined with a choledochostomy in one case. A choledochostomy, already mentioned, was done in one case with stone in the common duct.

THE PROGNOSIS OF DUODENAL ULCER

By MAX EINHORN

The prognosis of a disease runs parallel with its therapeutic possibilities. Progress in the cure of a malady improves its prognosis. In duodenal ulcer great advances have recently been made in diagnosis as well as in treatment. The outlook, therefore, for patients suffering from a duodenal ulcer is nowadays much brighter and more favorable than in former years.

With regard to prognosis it will be well to divide duodenal ulcers into the following groups:

(a) Simple duodenal ulcer;

(b) Duodenal ulcer accompanied by pylorospasm and usually also hypersecretion (alimentary or continuous);

(c) Duodenal ulcer accompanied by pyloric or duodenal stenosis;

(d) Duodenal ulcer with recurrent hemorrhages.

(a) Simple duodenal ulcer. Here the usual symptoms are epigastric distress two to three hours after meals; sometimes "hunger pain"; long periods of euphoria alternating with comparatively short periods of suffering. Gastric hemorrhage or melena may have occurred once.

This group gives a comparatively good prognosis provided that some form of a rest cure is rigidly carried out: rectal alimentation then von Leube-Ziemssen milk diet; or duodenal alimentation; or simply a milk and egg diet and rest abed for about two to three weeks. Later on no over-exertion (physical or mental) and a general hygienic way of living.

The oftener the attacks recur the more doubtful the prognosis becomes as to a complete cure by medical measures. Operative intervention (gastroenterostomy preferably with pyloric occlusion) offers a pretty good prognosis with regard to the future.

(b) Duodenal ulcer accompanied by pylorospasm and also hypersecretion (alimentary or continuous). Severe pains and frequent

vomiting are here the chief symptoms. Hypersecretion either alimentary or continuous is here constantly encountered. The gastric juice is usually hyperacid. When the pylorospasm reaches a higher degree slight ischochymia appears off and on. The prognosis of this group is quite severe under ordinary methods of treatment (alkalies, even milk diet). Duodenal alimentation gives a better prognosis. But in case the latter does not produce the desired effect in from two to three weeks, an operation (gastroenterostomy with pyloric occlusion) should be performed. The latter usually improves the prognosis.

(c) Duodenal ulcer accompanied by pyloric or duodenal stenosis.

Ischochymia is here constantly present. In cases of beginning pyloric stenosis; duodenal alimentation and then stretching of the pylorus may be tried. The prognosis under this mode of treatment varies in different patients. The condition must be watched and the prognosis made accordingly. Should there be no improvement, or in case the stenosis is further advanced, so that the duodenal bucket fails to pass through the pylorus, an operation (gastroenterostomy) should be performed. Barring the dangers resulting from the surgical intervention, the result is here usually very good, and the prognosis accordingly favorable.

In duodenal stenosis, when situated below the papilla of Vater, there is bile constantly found in the stomach or in the vomitus. The treatment requires surgical intervention and the prognosis then becomes pretty good.

(d) Duodenal ulcer with periodically recurring hemorrhages.

In this group the main predominating symptom is a profuse hemorrhage (either hematemesis or melena or both), which periodically returns and endangers the life of the patient. An interval operation (gastroenterostomy eventually with pyloric occlusion) gives the best results and renders the prognosis more favorable. The latter must, however, be made with caution, as there may be a new hemorrhage even after apparent perfect recovery from the operation. In the latter event the prognosis becomes doubtful and worse with each repeated hemorrhage.

In groups (b), (c), and (d) the prognosis, in case no surgical intervention be undertaken, must not be made too favorable, as there is a possibility of perforation. With the gravity of symptoms the liability of this event increases. Continuous hypersecretion and severe pains are frequently prone to perforation. Appropriate measures should then be taken, in order to make the outlook brighter.

THE POSSIBLE DEPENDENCE OF GASTRIC AND DUODENAL ULCER IN MAN ON A DISTURBANCE OF INTERNAL SECRETIONS

By G. A. FRIEDMAN

The explanation of a disease is plausible when the results of experimentation and clinical experience are in accord with the findings of the pathologist. However, since the pathologist has rarely the opportunities to investigate the changes that occur during the initial stage of an illness when the pathological lesions are first being developed, and since he deals in the majority of instances with alterations of tissues probably existing an entire life time and consequently when the disease is most advanced and the pathological changes so vastly modified by numerous factors, the suggestions as to the possible explanation of the pathogenesis of certain diseases may come from the experimentor and the clinician. This is apparently true in regard to the origin of gastric and duodenal ulcer, for lately it has been shown that the experimentor and the clinician have been the real investigators of this disease, and have rendered possible an explanation of the common cause of peptic ulcer in man by a study of internal secretions, based on experimental work which seems to harmonize with clinical experience.

It is beyond my province to discuss the theories that have been advanced to explain the pathogenesis of ulcer in man, but suffice it to say that not one of the explanations has been accepted as the common cause of ulcer, and this may be seen from a statement in a circular of the Special Committee in Germany for the collective investigation of gastric ulcer. "The nature of gastric ulcer," the statement reads, "has not yet been explained, even if some have been successful in producing it experimentally with all its characteristic signs. The etiology of ulcer in man is practically unknown." However, by our increased knowledge of activity of endocrinic glands, by our closer study of the anatomy and the physiology of the nervous system, by the careful investigation and observation of cases by the clinician who has had the opportunity of watching and studying individuals during the whole course of the disease, both medical and surgical, and by our improved methods of animal experimentation, knowledge of real value has been obtained. An attempt is, therefore, made to explain the pathogenesis of ulcer in man from a different standpoint.

Briefly mentioned, the theories that have been advanced in previous years, are the vascular, the neurogenous, the toxic and the microbic. Perhaps a few words should be said concerning the neurogenous origin of ulcer. It is a well known fact that ulcers or erosions of the stomach were obtained by cutting the vagus nerve, the sympathetic, or both. In Lichtenbelt's[1] experiments, the ulcers produced by vagotomy persisted without tendency to heal, and on account of the absence of this tendency, they greatly simulated the peptic ulcer. Still the neurogenous explanation of peptic ulcer never obtained due prominence, probably because the clinician did not appreciate the nervous symptoms found in individuals afflicted with ulcer, and because the pathologist was rarely able to discover changes in the nerves of his ulcus material. But we now know that a functional disturbance in one structure may produce pathological changes in another; and in seeking the origin of the initial lesion in peptic ulcer, we have met with many strong proofs, both clinical and experimental, which have led us to conclude that the lesion is due to a functional disturbance of the nerves supplying the parts involved. This functional disturbance of the nerves may probably arise from errors in internal secretion.

Due to an irritation arising from some source in the body, probably the disturbed secretions of the ductless glands, or produced by the injections of certain substances or drugs into the body, stimulation of one of the nerves leading to one or more of the smaller gastric or duodenal arteries, may develop a spasm of that vessel or cause occlusion of the vessel by a spastic contraction of the musculature surrounding it. The result from either of these possibilities is an ischemia of the gastric mucosa supplied by the vessel involved and thus, we have the initial lesion. Since cardiospasm, gastrospasm, pylorospasm, and hour-glass stomach are known to exist in individuals without the presence of an organic lesion as an ulcer, a primary irritative state of the vagus nerve, with the resulting gastric muscular spasm, cannot be denied. If such irritative conditions arising from functional disturbances in nerves are true for large areas of musculature, then it is probably also true for minute areas.

The explanation here set forth—that of spastic ischemia—must not be confused with the vascular theory by which an attempt is made to explain the origin of ulcer as arising from a stasis in the gastric vessels with the resulting changes in nutrition, or affliction of the blood vessels by disease, by embolic or thrombotic processes or by arteriosclerosis. It is true that these occasionally cause ulcer-

ation, but they are by no means the common causes. The theory that ulcer is caused by an irritation of the nerve leading to the smallest vessel causing a spasm of its wall, or even its occlusion by spastic contraction of the musculature surrounding it, either condition leading to an ischemia of the mucosa with subsequent ulceration, is favored by such men as Lebert,[2] and recently by v. Bergman,[3] Benecke[4] and others.

The organs which are supplied with smooth musculature as the stomach or duodenum, are under control of the vegetative nervous system, the regulation of which is partly independent of the central nervous system. Langley divided this vegetative system into the cranial-sacral-autonomous group, extended vagus, or the para-sympathetic group and the sympathicus proper. He also showed that the antagonistic physiological relation of both groups existed not only in the heart, where this antagonism was most evident, but was present in the stomach and intestines where, however, the vagus fibers caused stimulation of the smooth musculature and the sympathicus inhibition of peristalsis and secretion.

Langley's well-known teachings of antagonism have been strengthened by the researches of H. H. Meyer[5] who showed that certain drugs as pilocarpin, muscarin, physostigmin, and cholin have a selective action upon the autonomous nervous system and also upon the sweat glands. Atropin paralyzes this system. Adrenalin, however, has been shown to have a stimulating effect on the sympathetic nerves. There is as yet no known paralyzer of the sympathetic similar to the action of atropin on the extended vagus or autonomous system.

The vegetative nerve system supplies the glands of internal secretion as well as the viscera. The stomach is supplied by the terminal branches of the vagus. The duodenum is largely supplied by the sympathetic fibers and by some of the vagus fibers. The adrenals obtain their nerve supply almost entirely from the sympathetic through the splanchnic nerve. The thyroid, however, has a double innervation, the sympathetic and the vagus. The pituitary body may be excluded from consideration here since the secretion of this gland acts upon tissues innervated by the pelvic nerve.

There now remains the application of these physiological, pharmacological, and anatomical facts to the clinic and this was done by Eppinger[6] and Hess,[7] whose teachings of vagotonia and sympathicotonia are well known. They have clinically divided patients into two groups, the vagotoniac and the sympathicotoniac, basing their

classification upon the different symptoms arising from disturbances in one or the other of the subdivisions of the vegetative system. By a vagotoniac is meant an individual who is extraordinarily susceptible to drugs, stimulating or paralyzing the vagus nerve, as pilocarpin, atropin. Sympathicotoniacs on the other hand, are extremely susceptible to adrenalin, the stimulating drug par excellence of the sympathetic. The symptoms and signs belonging to each clinical group and the symptoms produced by the injection of the specific drugs mentioned, have been well described and need not be mentioned here. However, it must be remembered that no sharp lines can be drawn between the two groups, for often the symptoms overlap, but one should always consider the symptoms and signs related to vagotonia and sympathicotonia, as stigmata of the vegetative nervous system.

In order to make use of all the considerations mentioned, it must be shown that vegetative stigmata are actually present in the majority of individuals suffering from gastric and duodenal ulcer. Clinical experience shows that patients suffering from chronic peptic ulcer may be divided into two groups:—First, those in whom the organic element without apparent nervous manifestations is evident. At operations, ulcer is usually found. These patients are frequently benefited by the various surgical procedures. Secondly, those in whom the nervous element is so predominant that it is often difficult to eliminate the organic element as the chief cause of trouble. At operation, ulcer is found, but usually the result of the operation is not beneficial. If one questions these patients carefully as to symptoms and signs regarding the nervous system, autonomic and sympathetic, he will often be surprised as to the number of vegetative stigmata present, even in the majority of cases belonging to the first group. The complete absence of symptoms and signs pointing to a disturbed equilibrium of the vegetative nervous system may be mainly noticed in the fifth or sixth decade of life. The younger the individual afflicted with peptic ulcer, the more numerous are the vegetative stigmata. But even in old people, in whom the first symptoms of ulcer dates back twenty or twenty-five years, one will elicit the history of previous nervous symptoms which may be interpreted as evidence of vegetative disturbance. It is a well-known fact that functional disturbances have a tendency to disappear with age, though the organic lesion, the sequel of such disturbances may remain.

The symptoms and signs usually found in cases of peptic ulcer

are practically similar to those found in vagotonia and sympathicotonia, the underlying causative factor being the same, namely a disturbance in the vegetative nervous system. Gastric ulcer cases show frequently symptoms of vagotonia, duodenal ulcer cases more often symptoms of sympathicotonia. The chief symptoms elicited in the history are:—excessive salivation or dryness of the mouth, clammy or dry hands and feet, a tendency to perspiration, usually localized to some area, as the axilla, beneath the breasts, etc., constipation usually of the spastic type or rarely diarrhea. Among the more important physical signs and phenomena in ulcer cases suggestive of a derangement of the vegetative system we find narrow or wide pupils, various grades of protrusion of the bulbi, even exophthalmos, absence or diminished corneal reflex, narrow or widened polpebral fissures, excessive flow of tears and glittering eyes, gastric succorhea or achylia, high or low gastric acidity, gastrointestinal hyper or hypomotility, spastic or atonic constipation, bradycardia or tachycardia, absence or exaggeration of gag reflex, dermographia and Ashmer's oculo-cardiac reflex, which is produced by a continuous pressure with the fingers on the eyeball and noting the sudden slowing of the pulse rate, a sign of vagotonia. In addition, we can note in cases of peptic ulcer the presence of Stiller's habitus and as pointed out by E. Kraus,[8] the so-called Blähhals, a prominence of the neck due to an extreme vascularization of the thyroid gland.

Furthermore, the patients with peptic ulcer respond to the pilocarpin and adrenalin tests. Westphal[9] and Katsch,[10] who have made an extensive study of this subject, pointed out that some of these patients are more susceptible to pilocarpin and others to adrenalin, which fact proves the clinical findings of Eppinger and Hess. Only in the middle-aged patients they found frequently that the reaction was negative to either of these drugs. My own experience has taught me that individuals suffering from gastric ulcer present more often vagotonic symptoms and respond rather strongly to the injections of pilocarpin, while those suffering from duodenal ulcer show frequently the sympathicotonic symptoms and react therefore more often positively to injections of adrenalin. These facts are probably explained by the differences in innervation of the stomach and duodenum. We see, therefore, that clinically and pharmacologically the symptoms and signs which define the status of the vagotoniac and the sympathicotoniac may be found in patients suffering from gastric and duodenal ulcer.

There are, moreover, other factors which suggest the dependence of ulcer on the derangement of the vegetative system with the consequent disturbance in certain ductless glands. Several years ago, Dr. Lewis, of the General Memorial Hospital, assistant of Professor Benedict, at my request, has examined the percentage of blood sugar in a number of my patients whom I believed had peptic ulcers. Operative evidence was obtained in ten of them, and in five of these, callous duodenal ulcer was found. In these the percentage of blood sugar was above normal, while in four others who had pyloric ulcers, the percentage of blood sugar was below normal. However, in the tenth, in whom ulcer of the lesser curvature was found, the percentage of blood sugar corresponded to that found in duodenal ulcer cases.

The change in the percentage of blood sugar is, I believe, due to a glandular disturbance. That the product of the secretion of the islands of Langerhaus requires the presence of some other agent for its glycolytic action was first shown by Diamare,[11] and later by others. Sajous,[12] in 1907, suggested that the secretion of the adrenal was the necessary factor in this process. This was further substantiated by W. G. MacCallum[13] four years later.

Secondly, we have the characteristic differences in the blood pictures between chronic callous gastric and duodenal ulcers. These differences have been noted and pointed out by me in several of my published papers.[14, 15, 16, 17] But the significant fact is the resemblance of the blood count in duodenal ulcer to that of polyglobulia induced by adrenalin injections and of the blood picture in gastric ulcer to that found in hyperthyroidism. Bertelli,[18] Falta,[19] and Schweeger[20] and later Imachnitzky[21] have observed an increase of erythrocytes of from 30 to 100 per cent. in dogs and man after intravenous or subcutaneous injections of epinephrin (this experimental polyglobulia lasting sometimes for about 30 hours), and they have also noted after such injections a marked decrease in the eosinophiles. In my papers I show a polyglobulia and an eosinopenia to be significant of duodenal ulcer of the callous type. The similarity of the blood picture of pyloric ulcer to that of hyperthyroidism—a mononucleosis and a relative eosinophilia—is also quite marked. Kocher[22] has repeatedly stated that the mononuclear cells frequently predominate in Graves' disease. In addition, Eppinger[23] frequently found an increase of eosinophiles. I have observed in nearly every case of the callous pyloric ulcer an increased number of small mononuclears and an increase in the eosi-

nophiles. Although some state that in myxodema there is an increase in mononuclears, others believe that the picture found in this condition is not analogous to that in Graves' disease, because after the administration of thyroidin in myxedema, the blood picture returns to normal, while in Graves' disease it diverges still further from normal. It should be mentioned here that Kaufmann[24] who made blood examinations in a number of gastrointestinal disorders has found frequently lymphocytoses.

Although we have recently learned to associate sympathicotonic and vagotonic symptoms with disturbances in equilibrium of the vegetative nervous system and although we have seen that the occurrence of ulcer is frequent in cases of vagotonia and sympathicotonia, there remains the correlation of these facts with disturbances in internal secretions. It is well-known that the vegetative nervous system is the regulator of the glands of internal secretions as well as the viceral organs. Asher[25] and Flachs[26] have indisputably shown that the thyroid gland is influenced by the superior and inferior laryngeal nerves. Biedl,[27] Dryer,[28] Tsherboksaroff[29] and Asher[30] have in addition shown with absolute certainty that the splanchnic nerve is the secretory nerve to the adrenal. It appears that when one of the glands, for instance, the thyroid or adrenal, has been stimulated by the vegetative nerves and kept under its influence abnormally, there may be a reaction, and the nerve itself may become influenced through the disturbed activity of the gland; in other words, a vicious circle may set in between the vegetative nerve and the gland. Since, therefore, a disturbance in the vegetative nerve, vagus or sympathetic, may lead to disturbances in the function of the thyroid or adrenal, and since there is a reciprocal reaction between them, a minor degree of disturbance in these glands may show its influence upon the nerves, and the result of such influence may become evident clinically, by pathological changes in the structures supplied by the nerves affected, and by the production of the symptoms and signs of vagotonia or sympathicotonia. The mode by which the ductless glandular system may influence the excitability of the vegetative nerves is not quite known, but it is probably produced through the agency of hormones. At least this has been established with certainty in regard to adrenalin, and it is possibly true of the other internal secretions.

The vegetative stigmata found in individuals suffering from peptic ulcer, the susceptibility of these patients to the administration of drugs which have a selective action upon the vagus and sympathi-

cus, the blood picture of duodenal ulcer resembling the experimental polyglobulia and eosinopenia after adrenalin injections, the blood picture in pyloric ulcer which frequently simulates that found in hyperthyroidism, all these facts are hardly sufficient to lead us to a conclusion as to the possible dependence of ulcer in man on a disturbance of secretion of certain ductless glands. Thus far we know that an excess of adrenalin is circulating in the blood of the sympatheticotoniac. The excess of secretion which is supposed to circulate in the blood of the vagotoniac is not known. Eppinger and Hess have named this hypothetical secretion "autonomin" and this is supposed to stimulate the autonomous system. However, since the thyroid has two secreting components, one from the sympathetic and the other from the vagus, the component originating through stimulation of the vagus fibers may be the one circulating in the blood of the vagotoniac. The experiments of Westphal[31] seem to hint to such a possibility. He first tried to imitate vagotonia in rabbits, cats, dogs and guinea pigs by injections of pilocarpin. He succeeded in producing peptic ulcer of the stomach in nearly all of the rabbits, and in some of the cats and in dogs. I have repeated his experiments on rabbits and present here four specimens showing distinctly peptic erosions after pilocarpin injections. Since, after thyroidectomy, as it has been proven, pilocarpin had little effect in provoking vagotonic symptoms, we possibly have proof of the relation rather indirectly of some component of the thyroid secretion upon the vagus. This leads me to mention the so-called vagotonic type of Graves' disease. This has first been described by Eppinger and Hess who have shown that, although it is generally acknowledged that Graves' disease is due to a disturbance in the sympathetic, there are definite forms of Graves' disease with symptoms and signs pointing to a heightened tone of the vagus element supplying that gland.

We became more convinced that an excess of thyroid secretion may affect the mucous membrane of the stomach, producing erosions, since in two dogs and one rabbit (of four animals experimented upon by subcutaneous and intravenous injections for about one week of dessicated thyroid gland) we have obtained gastric erosions.

Seeing a possible connecting link between the polyglobulias and eosinopenia which I found in duodenal ulcer and the experimental polyglobulias found after injections of adrenalin on the one hand, and the tendency of adrenalin to affect tissues innervated by the

sympathetic on the other, we set up the working hypothesis that the initial lesion of duodenal ulcer may be caused by excessive secretion of the adrenals. With this object in view experiments were undertaken consisting of repeated injections of adrenalin in dogs. Since some of the experiments described here have been fully published in two of my papers, [32, 33] I need but mention them briefly.

It was found that injections of adrenalin administered to dogs intravenously, subcutaneously, or intramuscularly for about one to two weeks in dosages not exceeding three milligrams of the usual commercial solution (1:1000) are liable to cause lesions, erosions or superficial ulcerations in the duodenum. As such lesions were found in the duodenal mucosa in eleven dogs out of twelve and later in two out of four and only occasionally gross changes were noted in other organs, we concluded that adrenalin might have a preferential action upon the duodenum, probably because of the latter's rich sympathetic nerve supply, since as has been pointed out, the sympathicus. resp. splanchnicus is the secretory nerve of the adrenals. In normal dogs, autopsied as controls, the gastric and duodenal mucosa was found to be intact. In looking over the experiments with injection of adrenalin, in rabbits which were done previously for other purposes, we were surprised to find frequently notes of "marked congestion" or lesions in the first por tion of the duodenum.

After one-sided thyroidectomy in dogs and in rabbits, lesions or ulcers were found in the duodenum more frequently than in the stomach. Occasionally ulers were found in both viscera or in the jejunum. A careful search in the literature has revealed that Carlson[34] and Jacobsohn[35] have incidentally found gastric and intestinal lesions in seventy-five per cent. of thyroidectomized dogs. They emphasize the fact that the ulcers were always most extensive in the upper part of the duodenum.

After extirpation of both adrenals in two stage operations and after extirpation of one adrenal in dogs and in rabbits and also later in cats and in guinea pigs, lesions or erosions were frequently found in the stomach. In the duodenum of rabbits and guinea pigs and in one dog, lesions were found also after one-sided adrenalectomy, when the unextirpated adrenal became hypertrophied.

Gastric ulcers after exirpation of adrenals were first produced by Finzi.[36] He also showed that if after extirpation of the suprarenal gland, adrenalin is injected, the gastric mucosa remains intact.

Elliot[37] produced upon adrenalectomy, ulcers in cats, and recently Mann[38, 39], in dogs and in cats.

After extirpation of one adrenal and one thyroid lobe of the same or the opposite sides, no lesions in the stomach or duodenum were found in our experiments.

To sum up the results of my experiments presented in the two communications and from those yet unpublished, we have: 1. Adrenal insufficiency causes in various species of animals, lesions or ulcers in the stomach. 2. An excess of thyroid gland, as produced by repeated intravenous injections, was probably responsible for the gastric lesions in three animals out of the four experimented upon. 3. Thyroid hypofunction caused the appearance of duodenal and gastric lesions. 4. An excess of adrenalin produced by repeated injections of the drug, led to appearance of lesions in the duodenum of dogs and rabbits. 5. The simultaneous production of adrenal and thyroid hypofunction did not lead to any lesion in the stomach, nor in the duodenum of rabbits. 6. When after removal of an adrenal the other became occasionally hypertrophied, lesions were seen in both viscera in rabbits.

From our experiments it seems probable that gastric lesions may be dependent upon adrenal insufficiency as well as upon excess of adrenalin. Gastric and duodenal lesions may be dependent upon the alternating effect of hypo- and hyper-function of the adrenals. From all these considerations a correlation of secretions of the thyroid and adrenals seems to be plausible in the causation of gastric and duodenal lesions in our animals.

For the sake of briefness, I have to omit a discussion, presented in one of my papers as to reciprocal relations between the thyroid and the adrenals as obtained in our animals. In our thirty-six thyroidectomies performed in dogs and in rabbits, we have never observed hypertrophy of the unremoved thyroid lobe unless as happened in several dogs in which infection set in. But we did observe in two dogs and two rabbits after parathyroidectomy where parathyroids were not spared, a marked hypertrophy of the adrenals. These animals died from tetany. It is possible then, that after one-sided thyroidectomy, the adrenals hyperfunctionate without hypertrophy and in consequence duodenal lesions frequently develop as they do after injections of adrenalin. The gastric lesions after removal of the adrenals may be due to a hyperfunction of thyroid as occurs after injection of dessicated thyroid extract. Although, as has been mentioned, there is a vagotonic type of

Graves' disease, Higier[40] believes that Addison's disease also presents the best illustrative instance of a slowly developing vagotonia, emaciation, diarrhea, low blood pressure, and the reduction or disappearance of blood sugar. In classifying Addison's disease, therefore, as vagotonia, Higier sees the abolishment of the most important sympathetic impulses. If a vagotoniac type of Addison's disease is possible, what should be our conception of it? As Addison's disease develops, the sympathetic impulses become gradually abolished, since the normal tone of the sympathetic is under control of the adrenals. With the double innervation in the thyroid, the antagonistic vagus element in the gland, therefore, hyperfunctionates, and as a result an excessive amount of thyroid products, the so-called autonomins of Eppinger and Hess, will be discharged into the circulation. The effect, however, of this disturbance in secretion, may become modified by the presence of diseased adrenals. Just as there is a possible connecting link, therefore, between vagotonic exophthalmic goiter and Addison's disease, a somewhat similar correlation might have developed in our animals after removal of one adrenal and one of the thyroid lobes.

We now turn to the applicability of these experiments to the clinic. Since vegetative stigmata are found in the majority of patients suffering from gastric or duodenal ulcer, and since a disturbance of the equilibrium in the vegetative nervous system may lead to a disturbance in the secretion of the thyroid or adrenals or both, there is a possible connecting link between the vegetative stigmata and the appearance of the initial lesion of peptic ulcer. Although Eppinger and Hess were the first to recognize anomalies of constitution as dependent on a derangement of the vegetative nerves, it was Körte[41] who originally in a discussion at the XXXV Congress of the German Society für Chirurgie in 1906 correlated the anomalies of constitution with peptic ulcer. He then expressed his opinion that a local affection of the gastric mucous membrane might possibly bear some relation to the constitutional anomalies, the nature of which was unknown, and that these anomalies of constitution were the disturbing factors in the healing process of peptic ulcer.

However, the functional disturbance in the vegetative sytem must not necessarily lead to a pathological change in the ductless glands as in the vegetative organs. As often happens, an organ neurosis, gastric or intestinal, without organic phenomena may be the result. Hence we may also assume a ductless gland neurosis by which I

mean a functional derangement of the nerve supply to the gland without a pathological change in that organ or nerve but leading, however, to a disturbance in secretion. Bauer,[42] Hemmeter[43] and others dealt extensively with these neuroses of endocrinous glands. The secretion of such a disturbed gland may react upon the vegetative nerve system and influence the system still more, thus establishing a vicious circle as has been explained previously. Thes factors may lead to the anomalies in constitution which Eppinger and Hess and Körte have noted, and may also produce the initial lesion of the ulcer. With the return to normal conditions in the vegetative nervous system and in the glands, the anomalies in constitution may disappear but the ulcer, however, the material or pathological result of all these disturbances, remains, and may now proceed to heal. McCallum[44] points out that many ulcers in man heal spontaneously as may be judged from the scars at autopsies. All have seen at operations deep scars in the stomach or duodenum from healed ulcers. Ulcers heal, therefore, when the anomalies of constitution due to disturbance in the equilibrium of the vegetative nerve system, and hence in the disturbance of the glands, disappear, but the scar is the witness, however, that such a disturbance has existed. One may now comprehend why some patients do not show vegetative stigmata at the time of examination, but have all the evidence pointing to an organic lesion, and why such patients are fully benefited by surgical procedures.

If it be true that the initial lesion of peptic ulcer is due to anomalies of constitution then the occurrence of peptic ulcers in the newborn and in young, may be explained as congenital—that is to say the inheritance of the anomalous condition. Huber[45] has made a special study of the occurrence of peptic ulcer in several members of many families. He came to the conclusion that the occurrence is not rare. I have under observation a girl with gastric ulcer whose mother was operated for gastric ulcer one year ago. I am almost certain that the more we question our patients in regard to inheritance, the more frequently will we discover the presence of the ulcer running in the same family.

There is no doubt that chronicity of ulcer depends upon many factors. The healing process of ulcer is probably prevented in man by anomalies in constitution which are difficult to install in animals. The spastic ischemia results in the initial lesion. Through the corrosive action of the excess of hydrochloric acid the further development of ulcer occurs. The acidity plays undoubtedly a rôle as a

secondary factor. The fact that in peptic ulcer one may find normal acidity, hypo-anacidity or even achylia gastrica does not prove anything to the contrary. We know that the vagotoniac shows in his stomach hyperchlorhydria, but according to Eppinger and Hess the vagotoniac might become a sympathicotoniac in whom low acidity is usually found as a result of the change. Aschoff's[46] explanation that the chronic character of ulcer, its location, and its shape, depend primarily on the mechanical conditions and the prolonged contact with gastric juice at the physiologic points of narrowing of the stomach and also upon the mechanical friction and stress at the lesser curvature along which the ingesta travels to the pylorus, is probably true. He emphasizes that the chronicity of ulcer does not depend on primary disease of the blood vessels.

The question now naturally arises, since the acute gastric and duodenal ulcer, the initial lesions from which the chronic ulcers may develop, are produced experimentally through a disturbance of thyroid and adrenal, why are ulcers not found in Addison's disease, in myxedema or in exophthalmic goiter? As to Addison's disease one must say that gastric disturbances do occur frequently. There is a special gastric type in this disease. Ulcers probably do not develop because Addison's disease is in the majority of instances a tuberculous condition. That tuberculosis has little affinity for the stomach and the first portion of the duodenum may be surmised by the fact that tuberculous ulcers of the stomach or duodenum are extremely rare in spite of the fact that tuberculosis is a common disease. Moreover, in individuals with gastric or duodenal ulcer, the adrenals may be found affected, as seen from the pathological findings of Finzi,[47] who showed the adrenals to be markedly affected in five necropsies. I have seen several cases of Graves' disease in women in whom symptoms of peptic ulcer were present. I have also recently observed in two female patients who had been operated for exophthalmic goiter, developing later clear symptoms and signs of peptic ulcer.

The increased frequency of peptic ulcer is a well-known fact and this is certainly due to the mode of living—the hurried life, the quick lunches, the tremendous business worries, and generally the wear and tear of life. That this nervous tension may lead to disturbances in equilibrium of the vegetative system is beyond doubt. The relation of this disturbance to the hyper-, hypo- and dys-function of the thyroid and adrenals, and reaction of the secretions of these glands in turn upon the vegetative system with production of

constitutional anomalies, have been explained. The presence of ulcer in these cases, the production of ulcer experimentally under conditions similar to that found in man, point to the initial lesion of the condition as due to disturbances in internal secretions.

Although it cannot be denied that the causes of the initial lesions of ulcer are manifold, the explanation set forth, however, appears to be by far, the most frequent cause of ulcer.

REFERENCES

1. Lichtenbelt.—Quoted from Westphal.
2. Lebert.—Beitrag zur Geschichte und Aetiologie des Magengeschwürs. Berlin, Klin. Wochenschr., 1876, No. 39.
3. G. v. Bergmann.—Das spasmogene Ulcus pepticum. Münch. Med. Wochenschr., 1913. H. 4.
4. Benecke.—Ueber die hemorrhagischen Erosionen des Magens (Stigmata ventriculi), quoted from Westphal.
5. Meyer, H. H., and Gottlieb.—Die experimentelle Pharmakologie.
6, 7. Eppinger and Hess.—Die Vagotonic. Berlin, Hirschwald, 1910.
8. Kraus, F.—Quoted from Westphal.
9, 10. Westphal und Katsch.—Dass neurotische Ulcus duodeni. Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie, Bd. 26.
11. Diamare.—Quoted from Sajous.
12. Sajous.—The Theory of Internal Secretion. The Practitioner, February, 1915.
13. MacCallum, W. G.—Quoted from Sajous.
14. Friedman, G. A.—A hitherto undescribed form of polycythemia and its possible relation to duodenal ulcer, chronic pancreatitis and a disturbance of internal secretion (epinephrin). Med Rec., October 18, 1913.
15. Friedman, G. A.—Weitere Erfahrungen uber Polyzythaemie beim chronischen uncomplizierten Duodenalgeschwür. Arch. f. Verdauungs Krankheiten, xix Ergänzungsheft, 1913.
16. Friedman, G. A.—The value of polycythemia for the diagnosis of duodenal ulcer, based upon sixteen operatively demonstrated cases. Med. Rec., May 16, 1914.
17. The difference in the morphology of blood in gastric ulcer, duodenal ulcer, and in chronic appendicitis, based upon fifty operatively demonstrated cases. Am. Jour. Med. Sc., October, 1914.
18-20. Bertelli, Falta and Schweeger.—Ueber die Wechselwirkung der Drüsen mit innerer Secretion. Zeitschr. f. klin. Med., lxxi 23 and also lc 1.
21. Imachnitzky.—Quoted from Biedl. Innere Seckretionen, 1913, p. 491.
22. Kocher.—Quoted from Falta. The Ductless Glandular diseases. English translation by Meyers, Blakiston, Second Edition, p. 34.
23. Eppinger.—Quoted from Falta.
24. Kaufmann, Jacob.—Lymphocytosis as a sign of constitutional derangement in chronic diseases of the digestive tract. Jour. A. M. A., 1914. Vol. 63[1], p. 1104.
25, 26. Asher and Flachs.—Quoted from Bauer.
27-30. Biedl, Dryer, Tscherboksaroff and Asher.—Quoted from Bauer.

31. Westphal, Karl.—Untersuchungen Zur Frage der nervösen Entstehung peptischer ulcera. Deutsch. Arch. f. Klin. Med., 1914, Bd. 114, p. 327.

32. Friedman, G. A.—The experimental production of lesions, erosions and acute ulcers in the duodenal mucosa of dogs by repeated injections of epinephrin. Jour. Med. Research, 1915, Vol. XXXII, No. 1.

33. Friedman, G. A.—The influence of removal of the adrenals and one-sided thyroidectomy upon the gastric and duodenal mucosa; the experimental production of lesions, erosions and acute ulcer. Jour. Med. Research, 1915, Vol. XXXII, No. 2.

34, 35. Carlson and Jacobsohn.—Further studies on the nature of parathyroid tetany. Am. Jour. Physiol., XXVIII, 133.

36. Finzi, Otello.—Ueber die Veränderungen der Magenschleimhaut bei Tieren nach Nebennierenextirpation und über experimentelle erzeugte Magengeschwüre. Virch. Arch., ccxiv, December, 1913.

37. Elliott, T. R.—Some results of excision of the adrenal glands. Am. Jour. Physiol., 1915, xlix, 38.

38. Mann, Frank K. C.—A study of gastric ulcers following removal of the adrenals. Jour. Exp. Med., 1916, Vol. 23, p. 203.

39. Mann, Frank K. C.—A further study of the gastric ulcer following adrenalectomy. Jour. Exp. Med., 1916, Vol. 24.

40. Higier, Heinrich.—Vegetative oder viscerale Neurologie. Ergebuisse d. Neurologie und Psychiatrie, 1912, ii, Heft I.

41. Körte.—Quoted from Suzuki. Ueber experimentelle Erzeugung der Magengeschwüre. Arch. f. klin. Chirurgie, Bd. 98, 1912, p. 632.

42. Bauer.—Zur Funktionsprufung des vegetativen Nervensystems. Arch. f. Klin. Med., 1912.

43. Hemmeter, John C.—Hypertonicity and hypotonicity of the vagus and the sympathetic nervous system. N. Y. Med. Jour., January 17, 1914.

44. McCallum, W. G.—On the pathogenesis of chronic gastric ulcer. Am. Med., 1904, viii, 452.

45. Huber.—Ueber die Erblichkeit des Magengeschwürs. Münch. Med. Wochenschr., 1907, January.

46. Aschoff.—Ueber die mechanischen Momente in der Pathogenese des runden Magengeschwürs und ueber seine Beziehungen zum Krebs. Deutsche Med. Wochenschr., Vol. xxxviii, 1912, xxxviii, 494.

47. Finzi, lc.

VENOUS STASIS AND COLLOIDAL DIFFUSION AS ETIOLOGICAL FACTORS OF GASTRODUODENAL ULCER

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It is imperative that we should make a very marked distinction between those conditions which contribute to the formation of

ulcers, whether they be those of lowered vitality, congenital defects, or loss of antibodies that permit an ulcer to grow. It is one thing to have predisposing conditions, and it is quite another thing to find the exact causes that produce those conditions. These two are widely separated from one another. They are two great questions. Since 1900 my attention has been directed to a study of the question of what actually does produce ulcers, both in animals and in the human. I am familiar, as many of you know from my literature on the subject, (1) with the many failures to produce what we can recognize and call *true* peptic ulcer experimentally; however, it is to be noted that we have found that many conditions favor the production of ulcer. We find, for instance, that extensive burns will sometimes permit ulcers to occur.

It has now been found by surgeons that asepsis has almost entirely prevented those ulcers from occurring in the duodenum.

Monihan, in his work, says that seldom now do they fail in preventing organisms to develop. Other surgeons, again have taken up the question of stasis in the cecum as a result of which micro-organisms produced by certain changes, either by direct invasion or through their toxins, are the cause of gastric or duodenal ulcer. Dr. W. H. Barber, writing on "Duodenal Dilatability" says, "From the results in this series of experiments it appeared that increased dilatability of the cephalad duodenum followed complete obstruction of the terminal ileum; similar results have since been obtained on cats. It is illuminative to see that, dynamically, duodenal tone appears to be influenced by the tone of the terminal ileum." (2) Still other surgeons speak of ulcer originating from appendicitis, many regarding it as coming up by way of the venous channels, by retrograde embolism, and lodging in the duodenum or stomach, and thus producing ulcer. Now they have empirically carried out operations, and have found that when they remove these foci the ulcers disappeared and the patients got well, and that must explain some of these conditions, remembering always that empiricism in medicine merely starts the inquiry for more scientific and exact knowledge through research.

The work of Stoerck in emphasizing the part played by the status lymphaticus in ulcer is undoubtedly of value, because many people having ulcer likewise show this condition, but status lymphaticus cannot be called the direct etiological factor in the production of ulcer.

Let us again revert to empirical facts gained from long experience

in clinical work. It is known that uremic ulcers occur and many pages have been written discussing "Uremic Ulcers" by which is meant kidney disease. We know that a large amount of kidney disease is due to intestinal flora and we find that the intestinal flora produce a condition in the kidney similar to that found in gastric and duodenal ulcer, and there is no longer any question that we see in appendicitis, in stasis intestinalis, in conditions of the gall-bladder and gall-duct conditions exactly similar to those found in gastric and duodenal ulcer, and that these conditions are more or less directly influenced by the intestinal flora.

The study of intestinal flora has been of great interest to me. As you may know, I have been able to show, in my animal experiments, that when the intestinal flora were fed to animals, ulcers were produced without the addition of trauma or of any other injury. Now, I did not produce simply local, small erosions or small hemorrhages, but actual perforations. Many of you are familiar with the many presentations that I have made on ulcer during the last sixteen years. (3) An ulcer of this type in the first part of the duodenum, with perforation, after fourteen months of feeding with bacteria, that is a chronic ulcer, with thickening around the edge, cannot help but impress one with the relation between the intestinal flora and the ulcers that so consistently followed when the animals were fed as I have described. After six or seven months feeding with bacteria during which time the animals showed frequent irritation, and finally on opening them up, the finding of deep ulcer penetration through all the coats, not merely an erosion, led me to the conclusion that there was a very direct relation between the feeding experiments and these ulcers. But this is empiricism again, because simply feeding bacteria to animals and having ulcers occur does not bring us any nearer a solution of the actual mechanism by which ulcers are produced. So, it is necessary to carry out another line of investigation, namely, to determine, if possible, whether the micro-organisms act through the toxins that are liberated either through the death of these organisms in the intestines and their breaking down, or through acting on the food in some unknown manner producing toxins which are absorbed, or whether the micro-organisms themselves affect some areas in the stomach or duodenum.

The evidence that I have been able to deduce from my experimental work shows that no inflammatory process takes place; there is no infection whatsoever. When we inject any micro-organism into the veins, we find them lodged in the follicles, and when they

produce folliculitis, sometimes breaking down, the condition may look like an ulcer to the uninitiated; but that is not true ulcer. When we found hemorrhagic areas which we were able to produce by many means (many foreign proteins and different varieties of bacteria injected into the blood) we did not regard these as anything like ulcer or like peptic ulcer. But when we found that each coat was gradually penetrated until finally perforation occurred, we concluded that this was true ulcer, and we wished to know the mechanism occurring in those experiments that produced the condition.

It was found that when an animal was allowed to go into shock, or when any stasis of the splanchnic area was introduced as a factor, or after some surgical operation, that frequently on section, that the intestinal flora, the intestinal bacteria, would pass through the mucosa, between the cells, as though passing through a filter, and that they would march onward like soldiers between the gland cells up into the submucosa. (4) We followed the destiny of these organisms as they passed along the submucous tissue. In order to have this exactly and scientifically done, we decided to use fetal animals. This was done because the fetal animal is sterile and we can be certain that the micro-organisms that we find migrating along the cells are the ones that we have introduced.

In order to study the routes by which the intestinal flora migrated we injected a fetal pig with a culture of colon bacilli, or other intestinal groups, and we found that the micro-organisms would course up between the gland cells and never through a gland; that they would cross over the muscularis mucosa into the submucosa, and then pass toward the head, cophalar, until they reached the pyloric region. There we would find that, if left longer, they would pass into the liver, and locate in different areas in the liver, around the cells, always passing between the two walls of the common duct, the muscularis and the mucosa, and finally reaching the liver. We found that there was a direct route which these bacteria always took from the intestinal tract when they were introduced into various areas.

We then investigated the routes by which the intestinal bacteria migrated in the adult animal and found that under certain conditions they regularly passed through and migrated along the cells in the same manner as they did in the fetal animal.

My microphotographs show the route which the bacteria take and also the variety of lesions which they produced, and the venous

stasis that follows the reaction which they incite in the mucous membrane.

The peptic ulcer bearing area located within a few inches of the pylorus, cephalic and caudal, has excited the most intense curiosity and interest since the earliest discovery of ulcer. The prevailing conception that the gastric secretion determines this location fades away under experimental observation. In experimental ulcer increased gastric secretion is never found. The rule is that there is a greatly diminished secretion of hydrochloric acid and the ferments.

In this connection Lester R. Dragstedt, (5) writing on gastric juice in gastric and duodenal ulcer, says, "The digestive activity of the gastric juice is not the important factor in the delayed healing of acute ulcers of the stomach and duodenum and the consequent formation of chronic ulcers. Ulcers produced by the local injection of silver nitrate become subsequently infected with organisms, probably from the alimentary canal." Again Dragstdt says, "It is well known that lesions of the gastric and duodenal mucosa heal readily in the presence of active gastric juice. Small abrasions of the stomach mucosa, such as those following at times the administration of the stomach tube, are common, occasion no discomfort to the individual, and in the majority of cases heal without further sequelæ. Nevertheless, up to the present time, the medical and surgical treatment of ulcer has been based essentially on the theory that the gastric juice induces chronicity of these ulcers by digesting the exposed edges of the mucosa.

Rosenow (6) has attempted to produce acute and chronic ulcers in the stomachs of dogs by the injection of certain strains of streptococci, obtained from the depths of gastric and duodenal ulcers in man. He has also claimed that gastric and duodenal ulcers in man are usually infected, that the route of infection is by way of the blood stream, and that the primary focus may be in some distant part of the body (6). Without multiplying references to the literature I think we must be willing to admit that the theory regarding the rôle played by the gastric secretion in the production of ulcer must be abandoned and that we must search elsewhere for a tenable hypothesis as to the causation of gastric and duodenal ulcer.

If the acidity of the gastric juice is not the chief inciting factor in the production of ulcer we must seek elsewhere for an explanation. Several investigators have questioned the rôle played by bacteria. W. E. and E. L. Burge (6) from their experiments conclude that the decreased resistance of a circumscribed area of the

stomach to the digestion of the gastric juice is due to a decrease in the oxidative processes of the cells of the area, and that the resistance of the unicellular organisms to the digestive action of the proteolytic enzymes can be increased or decreased by increasing or decreasing the intensity of the oxidation processes of the organisms, but he has failed to show the relation of bacterial invasion to this oxidative process.

H. L. Celler and W. Thalhimer (7) describe their own experiments and review those of Rosenow and as a result conclude that it must be assumed that some cause is operative in certain cases of ulcer preventing the healing of defects in the gastric mucosa and is inoperative in others. Even though anhaemolytic streptococci are present in some gastric ulcers, they cannot convince themselves that these organisms have been proven as yet to be the factor which either initiates the ulceration or prevents healing.

My own experiments recently have shown that there is a diffusion of gacteria from the intestinal lumen into the wall at different levels of the alimentary tract. The laws which govern the passage of the bacteria are those that govern the passage of a colloidal suspension through a filter. The micro-organisms do not enter the blood vessels or lymph channels, but make their way between the cells of the mucosa, crossing the muscularis mucosa, passing into the interstitial tissues of the submucosa and meeting antibodies in this zone, where the bacteria are either destroyed, or their multiplication prevented by the antibodies formed in this area. Bacteria that are not destroyed in this submucous tissue diffuse along the walls between the muscular coat and the mucous membrance, passing in the cephalic direction. The laws that govern the direction which the bacteria take cannot always be understood. While passing upward in the direction of the venous and lymph channels, bacteria are never found in the lymph or venous streams, but migrate or filter between the connective tissue cells.

When the bacteria finally reach the region of the pyloric orifice the stream is stopped. An accumulation occurs as a result of the stoppage of this current. The histological slides give the appearance of a "log jam" in the accumulated mass of bacteria in different stages of disintegration.

The conditions that allow the bacteria to filter in and along the walls of the intestinal tube are many. The most important and determining factor is the alteration in the venous circulation of the intestinal tract (9). Atony of the intestinal walls associated with

venous stasis is one of the important causes which permits filtration of bacteria. Obliteration of the lumen of the intestines by ligation at different points is also effective in causing filtration of the bacteria, but this filtration depends more on the degree of the disturbance of the circulation than upon the mere obstruction. (Barber 2.) Trauma, catarrhal states of the mucosa and inflammation do not necessarily favor the filtration of intestinal bacteria. If vessels are tied off to produce stagnation of the blood supply, other changes taking place as leucocytosis, marked edema, round-celled infiltration, are not so effective in determining the passage of the bacteria into the walls as splanchnic venous stasis induced by shock, anaphylaxis, and other less violent conditions.

The penetration of the bacteria is not diffuse but occurs at selective points along the tube. The laws which govern the selection of the exact point where bacteria will filter through are analogous to the relation of a colloidal suspension to a colloidal substratum; or they may be paralleled by the adjustment of the filtered substance to the pores of the filter. The bacteria that pass into this submucous zone often show immediate bacteriolysis on crossing the mucularis mucosa. Specific antibodies are evidently formed in the submucous zones because of this destruction of the filtered microorganisms. Certain intestinal mirco-organisms, such as the colon-bacillus group, coming in contact with the intestinal secretions, acquire a relative immunity against the destructive effect of the lymph or serum in the submucous tissue, and therefore escape bacteriolysis. These continue their journey encephlad to the region of the pyloric orifice; here meeting much more powerful antibodies they are destroyed by the increased ferments in this area. Their destruction in any accumulated numbers results in the destruction of the tissue; necrosis and ulcer formation is inaugurated.

We have shown by titrations of the blood serum with suspensions of cell substance that, using anaphylaxis as the index, the cell substance was 200 to 1,000 times more powerful in antibodies than in the blood serum of the same animal.

We made another curious and remarkable observation which should be emphasized, namely, that in the walls of the duodenum the antibodies were so powerful that in solution of one to one thousand they would cause death when added to the intestinal flora injected into a rabbit, much more quickly than the antibodies from the lower part of the intestinal tract. In some portions of the intestinal tract, near the ileum, the antibodies begin to lose this remarkable power

of quickly destroying bacteria. The repetition of this experiment many times over has led me to believe that after the tying off of the duodenum there are antibodies that split up the proteoses and kill the animals (because of their strength and the power of the proteoses that are formed) as the result of splitting up of the proteoses by the ferments formed by the antibodies located in this region.

The fact that the ligation of the pyloric area causes death in the animal, while ligations in the lower tract are not fatal until starvation supervenes, is undoubtedly due to the fact of this greater increase in the proteolytic antibodies in the duodenal wall as compared with those of the lower intestine. Because of the formation of these antibodies in this zone and their action on the bacteria, the bacteriolysis, I have named it the *"Zona Transformans."* Colloidal suspensions other than bacteria will also cause an anaphylactic reaction and even death. For example Bateman found that raw egg white would cause intense diarrhea in dogs, cats, rabbits and men, but that if the dose was properly adjusted to the animal certain antibodies were formed, until finally a tolerance occurs.

The local changes that are seen to take place consist of an autolysis of the tissue cells combined with a venous stasis which shows marked dilatation of the veins and contraction of the arteries. The appearance of the tissue indicates what we understand by the generic term, acidosis and asphyxia of the cells.

Klotz has indicated the alterations that take place in the vessel walls as an asphyxia of the cellular elements (9). The intercellular metabolism is no longer possible. Wells mentions a waxy degeneration due to an increase or accumulation of acid from defective oxygen supply, which results in a fatigue condition of the muscle fibers. When this condition is completed telangiectasis occurs, due to the injuries to the vessel walls, especially of the venous radicals with a corresponding contraction of the arteries. The deficiency of oxygen contributes materially to this permanent loss of venous tone, as Hooker has shown (11) "oxygen is essential to the rhythmicity in vascular muscle, and also its maintenance of tone."

This is my explanation of why it is that the intestinal flora play so important a part in the production of ulcers. And this is not denying the part played by other factors, both in animals and in human beings, or other conditions that are favorable to their production. But I still maintain that when we have rendered the conditions favorable, we have not yet produced the exciting cause of what we call ulcer. All these experimental lesions which I have

produced by the injection of bacteria are not true ulcer, and in my own study of all these different processes I feel that these lesions produced by the diffusion of bacteria are more like ulcers because of the slowness with which they are produced, and because they pass through the various stages, producing clear perforations and finally death in the animals, and this to my mind indicates that we are working in the right direction, remembering that in all experimental work each individual adds but a small fraction to the great unknown. But nevertheless, I feel as strongly to-day, even more strongly, than when I first started this work sixteen years ago, convinced of the truth and exactness of my observations. I am very sure they have led me to a better understanding of the etiology of peptic ulcer located in the pyloric and duodenal regions and has furnished me with a more rational basis for the treatment of this condition. I feel fully warranted in making this statement because of the high average of good results that I have had since treating these cases along the lines which these investigations have suggested.

A review of the dietetic and other adjuvants in the treatment of ulcer which my experience has shown to be valuable have recently been published in the Medical Record. (June 24, 1916.)

A review of my clinical cases, covering a period of fifteen years, which have been treated with autogenous vaccines show a higher percentage of permanent good results, than the cases treated previously to that time without the vaccines. The ages of the patients to whom this method of treatment has been applied have ranged all the way from infancy to eighty years. I do not claim that the vaccines have been the only factor in securing unusually good results, but that the vaccines in combination with the other methods, *the combined system,* warrants distinctly favorable conclusions on the basis of a careful analysis of the data presented by 158 cases, in which complete data could be collected and a much larger number in which the data was more or less incomplete. While my conclusions are based on purely empirical results, as Gay remarks (Jour. A. M. A., Oct. 28, 1916, p. 1263), "Purely statistical methods of investigation must in more alert minds yield to comparative studies." I have attempted to place the experimental facts before you and they seem to have a direct relation to our clinical experience.

REFERENCES

1. Turck—Journal of the A. M. A., June 9, 1916, pp. 1753-63.
Turck—Transactions of the American Gastro-Enterological Assoc., 1914.
Turck—Journal of the A. M. A., October 7, 1899.
Turck—Medical Record, October 7, 1905.

2. Barber—Medical Record, October 14, 1916. Also annals of Surgery, October, 1915, pp. 433-440.
3. Stoerk—Deutsche med. Wochenschrifte, Vol. XXX, No. 11.
4. Turck—Transactions of the American Gastro-Enterological Assoc., 1914.
5. Dragstedt—Journal of the A. M. A., Feb., 1917, Vol. LXVIII, No. 5, pp. 330.
6. Burge—Jour. A. M. A., 1916, LXVI, pp. 998.
7. Celler and Thalhimer—Jour. Experimental Medicine, 1916, XXIII, pp. 791.
8. Ferannini—Jour. A. M. A., Feb. 24, pp. 668.
9. Klotz—Jour. Medical Research, March, 1915, Vol. XXXII, No. 1, Whole No. 149, p. 27.
10. Hooker—Journal of Physiology, Vol. XXXI, No. 2, Nov. 1, 1912, p. 47.
11. (See 9.)
12. Bartholomew—Medical Record, August 19, 1916.
13. Spiethoff—Medizinsche Klinik, Berlin, Nov. 26, 1916, XI-XII, No. 48, p. 1252.
14. Turck—Illinois Medical Journal, Vol. 13, No. 6, pp. 631-634.
15. Richardson—Medical Record, Feb. 17, 1917, p. 293.

DISCUSSION:

DR. J. C. HEMMETER, OF BALTIMORE: A discussion may be constructive or destructive, and unless we have some criticism we shall drift into that state which is known as a mutual admiration society. I am sorry that Dr. Deaver left. I invited him to stay and hear me jump all over him, but he said he was used to that sort of thing and he preferred to go. So I will not discuss Dr. Deaver's paper. I heard only the last part of it. I did not hear the papers of Dr. Friedman and Dr. Turck. I am not convinced from the specimens that Dr. Friedman passed around, or from his microscopic projections on the screen that he is dealing with that which clinicians and pathologists call a typical duodenal ulcer. Dr. Friedman was very careful to speak of lesions and not of ulcers. I think that is a very fine distinction. The rabbit that showed a duodenal erosion fifteen days after the removal of one adrenal, showed simply what I call a hemorrhagic erosion, one of those predisposing states that might perhaps lead to a duodenal ulcer. It is not very clear to me why the removal of one adrenal should cause this lesion when the remaining adrenal is there to take up the function of its lost mate. We know from physiology and pathology that the removal of one organ can be replaced by the hyper-functioning of another. There is a paper on that subject in the November, 1917, number of the *Experimental Medicine Journal,* by Dr. Geo. N. Stewart, of Cleveland, Ohio. It is not clear to me why the removal of one adrenal should cause this lesion when the other is there to do its work.

Certainly there cannot be any absolute exclusion of function. That we find lesions in the duodenum after skin burns is intelligible from the deductions and inferences made by Vaughan and Edwin C. Faust; the latter produced a typical ulcer by the injection of a toxin he called "sepsin" gained from putrecent yeast, and Vaughan by injections of arsenic. These substances are injected under the skin. The dead, burnt skin produces toxins, and if the bile is analyzed for sepsin or arsenic, after the hypodermic injection of this metal or toxin, you find sepsin or arsenic in the bile. It is very highly probable that the excretion of these toxins into the duodenum through the bile can so poison the duodenal epithelium as to cause its destruction; later the autolysis goes deeper. What I call the duodenal or gastric ulcer is the typical histologic picture that Rokitansky first described so graphically, not simply the surface deformations of the columnar epithelium. One of the specimens that Dr. Friedman showed did not go any deeper than to the muscularis muscosae.

I also fail to understand the application of the word "Vagotonia," which means hypertonicity of the Vagus, to Basedow's disease. The cardinal symptom of Basedow's disease is fast heart. In Tachycardia we cannot logically speak of Vagotonia. If there is an excessive tonus of the Vagus we ought to expect Bradycardia.

Then the further hypothesis which ascribes a distinct anatomical picture—an ulcer, for example, in the duodenum—to the sympathicotonia, and another similar lesion only a half inch away from it in the pylorus to Vagotonia, is not clear to me.

I am very favorably impressed with the scholarly work of Turck. I have gone very thoroughly into a critical examination of his slides and they give evidence of a perseverance and patience that is most exemplary. We have in the two efforts of Friedman and Turck two entirely distinct tendencies. Friedman attempts to explain the production of duodenal ulcer by a chemical process; Turck by a bacterial process. Through the production and destruction of bacteria chemical conditions are produced, and a new rôle is assigned by Turck, and a very interesting rôle, to the sub-mucosa which he calls the *Zona transformans*. In their migrations through the epithelium the bacteria do not take the route by way of blood vessels or the lymphatic vessels. They permeate between the cells, and meet with their dissolution either by action of enzymes or by other processes in the sub-mucosa, which he regards as an organ designed for that very purpose; a very interesting and profound conception.

Dr. J. Kaufmann, of New York: As long as this is a congress of internists, I think we cannot let Dr. Deaver's remarks pass entirely unanswered. Dr. Deaver made some very strong statements.

I shall not discuss the main topic of his paper, the diagnosis. I will only point out that a diagnosis based exclusively on the so-called characteristic subjective symptoms is entirely unreliable. I have seen too many cases where a positive diagnosis on such a basis was made and where at operation no ulcer was found. Dr. Deaver actually dared internists to treat duodenal ulcer, threatening that we have to take all the responsibility for whatever happens to any one having duodenal ulcer. Gentlemen, I am willing to take that responsibility. I feel that when I advise a patient to undergo an operation the responsibility I take upon me is oftentimes very much more serious. The surgeon would be entitled to make the statement that Dr. Deaver made if he could show us that surgical treatment of duodenal ulcer accomplishes a permanent cure; but I am sorry to say that that is not so. I may mention here as a historical fact that exactly thirty years ago, in the winter of 1886, the first patient ever operated upon for gastric ulcer was a patient of mine, when I was an assistant at Kussmaul's clinic. Since then I have had opportunities to follow cases of gastric and duodenal ulcer operated upon on the other side of the water and here, and operated upon by the most illustrious surgeons, and have seen the results. I can only judge by the results obtained in my own cases, and I must confess that in a high percentage of cases the final results were poor. I used to be a very enthusiastic advocate of surgical treatment, but the frequent observation of poor immediate and poor final results have made me more and more conservative. Now, I think twice before I have a patient operated upon. Without discussing the indications for surgical treatment, I only wish to say that, generally speaking, the indication for surgical treatment comes up when medical methods fail, when the ulcer proves intractable. We cannot admit that operation per se is the paramount treatment of ulcer cases, because no operative procedure, not even the resection of the ulcer itself, removes the pathological condition which caused its formation and may give rise to new disturbances. I think Dr. Deaver, like most surgeons, is under the misapprehension that the anatomical changes which they find in opening up a patient are the "whole show," to use a slang expression. It is not so by any means. The anatomical changes which are found in the stomach or duodenum are effects of the pathological

process and not the cause. They may become contributory factors, but are never the original cause. Dr. Friedman in his very interesting paper struck upon the right road. I think we shall come to an understanding of the pathogenesis of peptic ulcer if we study more physiological pathology instead of relying entirely upon anatomical pathology. Dr. Friedman's suggestion is a very interesting one. At present I am not in a position to judge its value, but I shall certainly take it up and see whether there is any such possibility of differential diagnosis between duodenal and gastric ulcer on the basis of different disturbances in the vegetative nervous system possibly brought on by disorders of the internal secretions.

I would like to refer to one more statement which Dr. Deaver made. He said, and the observation is correct, that most of those patients have their attacks of annoying subjective symptoms either in the fall or in the spring, at all events, periodically, and he correctly emphasized that they are perfectly free of symptoms during the interval. Now, gentlemen, if the anatomical changes are the cause of the symptoms, why is it that these patients are free from symptoms for long periods, a whole year and more, while the anatomical changes, the defect caused by the ulceration, the adhesions, etc., remain practically unchanged? There must be something else which provokes the symptoms, and think that the disorders of the vegetative nervous system, whatever may bring them about, are the real cause of the periodical upset as well as of the original development of the ulcer.

Now, regarding Dr. Hemmeter's remark, I do not think that we need to make such a sharp distinction between the physical and chemical aspect as expressed in Dr. Friedman's paper, and the bacteriological view followed by Dr. Turck in his most interesting investigations. We need them both. It is very well possible that physical and chemical disorders brought on by disturbances in the vegetative nervous system, create that condition of lowered vitality in the gastro-intestinal tract which then gives the bacteria an entrance into the system, and that then with the persistence or rather the periodicity of the disorders of the vegetative nervous system, we get what finally is ulcer. I think this is a very important point, and that it also applies to Dr. Hemmeter's criticism of Dr. Friedman's findings. We are not able to reproduce the ulcer as we find it in the human being, because we cannot reproduce the periodical upset of the vegetative nervous system caused by disorders of the internal secretions.

Dr. J. R. Verbrycke, of Washington, D. C.: It seems to me unwise to accept the surgeon's criteria for diagnosis. His viewpoint and methods are altogether different from ours. In the first place, he sees ulcers which are of only one class—they are chronic ulcers. We also unfortunately see chronic ulcers, but we also see many others. The internist is not to blame because the surgeon sees the ulcers after many years of duration, as Dr. Deaver says himself, but partly the patient and partly the general practitioner. The surgeon attempts to make a diagnosis of cancer of the stomach before typical symptoms appear, and yet, on the other hand, in the diagnosis of ulcer of the duodenum he bases his diagnosis on a typical case, or what he calls a typical case. Now the surgeon's diagnostic viewpoint is mainly from the symptomatic side. The internist believes in using the symptoms, the physical examination, and every clinical sign which is at his disposal, and by so doing, I believe that the internist, when he is able to give this complete examination, is able to diagnose over ninety per cent. of the duodenal ulcers, and that he can do it before they get to their chronic stage. Duodenal ulcer represents the only dyspeptic condition which we can with any certainty in some cases diagnose from symptoms alone. Even then it is not advisable in those typical cases to make a prognosis or operate or treat medically without a more complete examination, if possible, because mistakes can occur both ways. There are many typical cases which do not give the typical periodicity and so forth. On the other hand, I have seen other cases which before operation gave clinical pictures of typical duodenal ulcer and which were due to adhesions from the gall bladder to the duodenum and the contraction of the duodenum by means of these adhesions, giving hunger pain. I have also seen similar symptoms occur from contraction by an adherent omentum, an omentum adherent in the pelvis in two or three cases. So that in direct proportion to the completeness of our examination will our results vary. I believe that the internist is able to make a better diagnosis before operation than the surgeon is at the time of operation. This brings us to the question of unfound ulcers, which I cannot go into at this time, but of which I could cite case after case. Nor can I take the various means in detail by which the internist does make his diagnosis of duodenal ulcer. Just a word about prognosis. When the surgeon can show us a larger proportion of cases cured after fifteen years than Joslyn shows of forty per cent. after surgery and thirty-eight per cent. after medicine, we

will have our cases operated on more often. But certainly these statistics showing only forty per cent. cured after fifteen years under surgery, and thirty-eight after medicine, shows that there is something decidedly unsolved by our present treatment, and that there is a lot for us to live for yet in the treatment of ulcer.

Another thing, the surgeon in his estimation as to whether the case is cured or not goes, as in his diagnosis, usually on symptoms. He writes to the patient, "Are you free from symptoms?" The patient may be free from symptoms, but oftentimes for months and years afterwards, if examination is made, the stools will be loaded with occult blood. He still has a little keg of gunpowder, just the same as he did before he was operated on.

Just one word more in closing. I would like to call to the attention of Dr. Friedman, when he speaks of the inherited tendency to ulcer, that I have published a report of two cases of what I call ulcer families with hereditary predisposition to ulcers in one family, in which the mother and three children were proven to have ulcers; and in the second, the mother and two children; and I know one other ulcer family which I have not reported.

Dr. J. W. Weinstein, of New York: I am purely a medical man and not a surgeon, but I must say that when it comes to the diagnosis of a duodenal ulcer I side with Dr. Deaver and with all the other prominent surgeons who hold exactly the same view that Dr. Deaver holds. Now we all must admit that the diagnosis of duodenal ulcer has undergone very radical changes. We all must admit that a few years ago medical men did not know how to diagnose duodenal ulcer. It was considered a feat. It was considered an effort worthy perhaps of a great medical man. In fact, we did not know at all the great frequency of duodenal ulcer. To-day, this is a diagnosis that is in the hands of every tyro. Now, Dr. Deaver told us how to do that. I think perhaps that medical men look for something difficult, for something complicated, and when something plain is handed over to them it seems they do not care to take it. Now, when a patient complains of pain, of oppression in his chest or in his stomach, coming on three, four or five hours after a meal; if he has got with those pains perhaps heartburn, belching, sour eructations; if those symptoms are relieved by ingestion of food; if they are relieved by vomiting; that patient has a duodenal ulcer. Now, Dr. Deaver has cited hundreds of cases. Dr. Munyon has cited hundreds of cases that he has operated on. Dr. Mayo and all

of the prominent surgeons in the country testify to that, and I really see no reason why we should not give heed to it.

The periodicity is also a very important point. When we find a patient tell us that he gets dyspeptic perhaps for a few weeks once a year, perhaps two or three weeks a year, a diagnosis of duodenal ulcer is probably right.

While I side with Dr. Deaver on the diagnosis of duodenal ulcer, I differ with him and hold with my colleagues on the treatment; because if any one would ask me what is the disease I can treat better than anything else I would say unhesitatingly that I can treat duodenal ulcer with better success than any other intestinal disease. I used the method a little over five years ago; I read a paper on it, and it has stood the test of time.

Dr. W. J. Mallory, of Washington, D. C.: On the question of the diagnosis of ulcer I think that what surgeons neglect to remember is that before cases come to them they have come out of the doubtful class; and that the surgeon sees more of the typical cases that are easier to diagnose, and also the class of cases which need surgical treatment. Until we find an actual exciting cause for ulcer, and it seems that Dr. Turck's paper is certainly on a very suggestive line of investigation, we are face to face with the problem as to what we shall do with our patients who present the well-known symptoms of gastric or duodenal ulcer—what the treatment shall be. My opinion is, in the light of what we have heard, that our treatment for those conditions is medical, unless complications have developed, and then it is, that the lesions are so marked, so definite, that they set up a new train of symptoms that are so disturbing that they must be rellieved by surgical means.

One last point: When the diagnosis is correct and the operation has been performed, and the patient has been treated in the hospital, and dismissed cured, he still has, as Dr. Verbrycke says, his keg of powder with him. He still has all of those predisposing causes that produced his gastric ulcer and some of his physical symptoms and disturbances, and he is still to be guided in a medical way or he will soon be a sick man again.

Dr. W. H. Stewart, of New York: I simply want to go on record in favor of the Roentgen diagnosis of duodenal ulcer. Dr. Deaver's statistics of two hundred cases with one hundred and ninety-two typical and only eight atypical, does not agree with my observations

in this locality. Those that I come in contact with show at least fifty per cent. atypical. In mose of the typical cases I should place the clinical history as No. 1 and the Roentgen findings as No. 2; but in the atypical cases I believe the Roentgen examination is the most accurate means of diagnosis, and I should place it as No. 1. We have absolute objective signs of duodenal ulcer in the majority of cases. I do not mean to say in one hundred per cent. by any means, but I believe my statistics will show something like ninety per cent. of correct diagnoses in all cases. I am sure that in many we have vague symptoms from obscure lesions in the right upper quadrant which are not so easy to "clear up" as Dr. Deaver would lead us to believe.

Dr. J. C. Hemmeter, of Baltimore: I would like to ask the gentleman whether he does ascribe more importance to the exact clinical history than to the radiograph?

Dr. W. H. Stewart, of New York: I said in typical cases, Doctor. I believe I would place the clinical history as No. 1 and the Roentgen findings as No. 2; but in the atypical cases I would place the Roentgen findings as No. 1.

Dr. M. Cross, of New York: I would like to ask Dr. Friedman if he was looking for these lesions in other parts of the body, in the intestines, heart, etc., and whether he found them.

Dr. G. Lenox Curtis, of New York: In 1892, I found that specimens of fresh syphlitic sores and those of early cancer growth, appeared practically the same under the microscopic, and later, that the blood of all cancer patients contained crypta-syphlitica.

In 1906 a paper by me claiming syphilis to be the etiology of cancer, appeared in the *New York Medical Record.*

I place all my cases under anti-syphlitic treatment, and all recover. But where it is possible to inject into the growth an astringent which ligates the blood vessels entering it, I do so, with the result that the growth is exfoliated, and the wound fills in with healthy tissue. I have practiced chemical surgery in this class of cases for 17 years and believe it to be the best known method.

Dr. G. A. Friedman, of New York: I wish first to reply to Dr. Hemmeter. At the start I want to make it clear that I did not

intend to demonstrate to you typical ulcers or chronic ulcers which you see at operation. This was not the purpose of my paper, nor of my work. I am dealing practically with the initial lesion, the explanation of which is by far more important than the factors which help to develop the ulcers from the initial lesions. Suppose some investigators, as I have recently seen, succeeded in producing chronic gastric ulcers by injections of nitrate of silver. It is self-evident that nitrate of silver cannot be the cause of the ulcer in man. In my paper I simply wanted to state, and to emphasize the possibility of the initial lesion of ulcer as dependent on a disturbance of internal secretions. I have therefore dealt with the vegetative nervous system. I have shown its relation to the thyroid and adrenals and to anomalous constitutions.

I have brought out the effects of the disturbances in the secretion of these ductless glands on the nervous system itself producing the various clinical types of patients with ulcer. I have explained in detail how the initial lesion, ischemia of the gastric or duodenal mucosa, may develop from a spasm of the smallest arterioles or from spasm of the muscularis by an irritable condition of the vegetative nerves. Then with the other contributive factors a typical chronic ulcer may result. I have stated in my paper that after extirpation of both adrenals the lesions are much more pronounced than after extirpation of one adrenal, but nevertheless you find lesions after extirpation of one to a somewhat less marked degree.

In regard to Dr. Hemmeter's remarks that if one adrenal is extirpated the other hypertrophies, I must say that this is frequently not the case, for in many cases after one-sided adrenalectomy, the unextirpated adrenal is not found larger. However, hypertrophy of the remaining adrenal does occur and especially so in guinea-pigs. There are usually no accessory adrenals.

Secondly, I would like to clear up the question of the so-called vagotonic type of Graves' disease. This is not my work, but the work of Eppinger and Hess, who distinguish between the sympathicotonic and vagotonic form. It is said by these authors that in the latter type there is a slight degree of tachycardia and other signs pointing to an irritation of vagus rather than of the sympathicus.

As to the last remark of Dr. Hemmeter why individuals afflicted with duodenal ulcer should present more sympathicotonic symptoms, and individuals afflicted with gastric ulcer more vagotonic symptoms, I cannot give a definite answer. But it seems to me that the reason

may be that the sympathetic nerve element is more pronounced in the duodenum and the vagus element in the stomach. The soil of the duodenum may also differ from the soil of the stomach. It is rather peculiar than cancer is so frequent in the stomach and so rare beyond the pyloric vein in the first portion of the duodenum.

Dr. Kaufmann's question is practically answered by my remarks to Dr. Hemmeter. As to Dr. Gross's question, in regard to whether lesions were found in other parts of the body, I have stated in my previous papers that lesions were occasionally found in other abdominal organs, but were not nearly as constant nor as pronounced as in the stomach or duodenum. Occasionally lesions in the appendix were found, and I myself have made notes of such cases. This would in addition show the relationship possibly existing between a disturbance of internal secretions and the appendix. And as a matter of fact, we really do not know as yet the cause of appendicitis.

Dr. F. B. Turck, of New York: I regret that the discussion did not take up more definitely the ideas of etiology, of pathology itself, from a phyiological and pathological standpoint. We would expect that from a society of internists, who ought to be most interested in it above all things; for remember, gentlemen, in this great question is involved not alone the problem of duodenal ulcer; there is involved a higher and a greater problem than this: Why we don't destroy ourselves; and I have attempted in my investigations to ask the question, not why we do not destroy ourselves, but why are we not all destroyed? Why does an ulcer form, is one question, but why we are not destroyed is another great question. This autolysis that is going on is a normal process. Why does it become pathological in a localized area? We must revert back again now and then to the empiric facts that are gained from long experience in clinical work. It is known now that uremic ulcers occur; many pages are given by Moynihan to the presence of uremic ulcers, meaning kidney disease. We know that a large amount of our kidney disease is due to our intestinal flora, and we find that the intestinal flora produces the same condition in the kidney that we sometimes find in ulcer conditions, so that in appendicitis, in stasis intestinalis, in conditions of the gall-bladder and gall duct we see similar processes and lesions.

The effect of the data given by Dr. Friedman is very illuminating

and very valuable, and we must consider that there are certain conditions which permit the condition he describes to exist. I have chosen for my part, this attempt to enlighten us a little more upon the relation between the intestinal flora, and I am more convinced than ever, as I said before, that we have here an opportunity for further and wider investigation. Much of this will depend upon some of you who are interested sufficiently in the great problem; for internal medicine hangs on many of these questions. We cannot go into such investigations, but there is no barrier against it if you want to undertake it.

CONSTITUTION

ARTICLE I

This Organization shall be known as The American Congress on Internal Medicine.

ARTICLE II

The objects of the Congress shall be: To promote the advancement of the science and practice of medicine, to further the study of biological medicine among its members, to elevate the standard of preliminary education of physicians and the standing of medical education, and secure enactment of just medical laws by the State and Federal Governments and of a Federal Law providing for a national medical license, to obtain the establishment of a National Board of Health, to promote friendly intercourse among physicians, to enlighten and direct public opinion in regard to the great problems of health and medicine, and to unite those working in the domain of internal medicine, to secure recognition for the term internist as the proper designation for such workers and to obtain proper scientific and material recognition of their work.

ARTICLE III

The Congress shall meet annually at such time and place as the Council may determine. Twenty-five members shall constitute a quorum.

ARTICLE IV

SECTION 1. The officers of the Congress shall consist of a President, a Vice-President, a Secretary-General, a Treasurer, and twenty-five Councilors, who with the officers shall constitute the Council, all to be elected from the active membership by ballot at an annual meeting, a majority of whom shall reside in the City of New York or its vicinity, excepting that the Secretary-General shall be elected for a term of ten years.

SEC. 2. The Council may be convened at any time by the President at the request of any five of its members. Its decisions shall be equivalent to acts of the Congress, and shall be reported to it at its next regular meeting. The Council shall constitute the nominating committee of the Congress.

SEC. 3. A vacancy occurring in any office may be filled by the Council.

ARTICLE V

SECTION 1. Any qualified physician engaged in the general or special practice of internal medicine or in laboratory research pertaining to it, may be proposed for fellowship.

SEC. 2. Applications for fellowship in the Congress should be made in writing to the Council. Five negative ballots shall reject an applicant.

SEC. 3. Applications for fellowship shall be accompanied by the annual dues of five dollars.

SEC. 4. Resignation of fellows shall not be accepted until all dues have been paid.

ARTICLE VI

All proposed changes in the constitution must be offered in writing at a regular meeting of the Congress. They are to be considered only at the next annual meeting when a two-thirds vote of the members present shall be necessary for their adoption.

BY-LAWS

ARTICLE I

The President shall preside at the annual meeting of the Congress and deliver an address, and shall be the chairman of the Council. In the absence of the President, the Vice-President shall preside.

ARTICLE II

The Secretary-General shall keep a record of the transactions of the Congress, and the Council, and committees, conduct all correspondence of the Congress, and mail to each fellow a program of the meeting at least two weeks in advance of the date thereof. The records, publications and seal of the Congress shall be in his custody.

ARTICLE III

The Treasurer shall collect all moneys due the Congress, disburse the same as directed by the Council, keep a proper account of all his transactions, and render an annual statement to the Congress. He

shall have charge of all property belonging to the Congress not otherwise provided for. He shall give bonds for the faithful performance of his duty, in such sum as shall be determined by the Council.

ARTICLE IV

The Council shall constitute a standing committee to consider all matters of interest to the Congress. It shall appoint all committee and conduct all business affairs of the Congress. It may, in its discretion, organize special scientific and local sections of the Congress.

Five members of the Council shall be elected annually by the Congress, each to serve for a term of five years.

ARTICLE V

Charges against any fellow must be made in writing. They shall be referred to the Council for investigation and action.

ARTICLE VI

The annual dues shall be five dollars, payable before the annual meeting.

ARTICLE VII

The order of business shall be as follows:

(1) Reading of the minutes of preceding meeting.
(2) Reports of officers, of the Council and committees.
(3) Presentation of communications.
(4) Miscellaneous business.
(5) Election of officers for the ensuing year.

FELLOWS OF THE AMERICAN CONGRESS ON INTERNAL MEDICINE, 1916-1917

Aaron, Charles O., Detroit, Mich.
Acuff, S. D., Knoxville, Tenn.
Ager, Louis C., Brooklyn, N. Y.
Alsop, Thos., Atlantic City, N. J.
Amster, J. Lewis, New York City.
Anders, James M., Philadelphia, Pa.
Arneill, James Rae, Denver, Colo.
Aten, William H., Brooklyn, N. Y.
Atkin, S. J., Brooklyn, N. Y.
Attshul, H., Hartford, Conn.

Baar, Gustav, Portland, Ore.
Babcock, Robert H., Chicago, Ill.
Bacon, Theo. T., Springfield, Mass.
Baketel, H. S., New York City.
Bangs, Charles H., Boston, Mass.
Barach, Jos. H., Pittsburgh, Pa.
Barnes, James, Chicago, Ill.
Barnes, Noble P., Washington, D. C.
Bartley, E. H., Brooklyn, N. Y.
Bate, R. Alex., Louisville, Ky.
Bathurst, Wm. R., Little Rock, Ark.
Beck, Harvey G., Baltimore, Md.
Beling, C. C., Newark, N. J.
Bell, John M., St. Joseph, Mo.
Benedict, A. L., Buffalo, N. Y.
Berg, G. F., Pittsburgh, Pa.
Berger, Samuel S., Cleveland, O.
Bettman, Henry W., Cincinnati, O.
Betts, Lester, Schenectady, N. Y.
Beyer, Louis J., Buffalo, N. Y.
Biddle, Andrew P., Detroit, Mich.
Bieber, Joseph, New York City.
Billings, Fredk. T., Pittsburgh, Pa.
Bishop, Ernest S., New York City.
Bishop, James, New York City.
Bishop, L. F., New York City, N. Y.
Bloch, Leon, Chicago, Ill.
Blackwood, A. L., Chicago Ill.
Bohan P. T., Kansas City, Mo.
Bonney, Sherman G., Denver, Colo.
Bosworth, Robinson, St. Paul, Minn.
Bowen, William, Knoxville, Tenn.
Briggs, L. Vernon, Boston, Mass.
Brockway, Robt. O., Brooklyn, N. Y.
Brooks, Harlow, New York City.
Brown, Alex. G., Richmond, Va.
Brown, Samuel S., Brooklyn, N. Y.
Buesser, Fredk. G., Detroit, Mich.
Bumsted, C. R., Newark, N. J.
Bunker, Henry A., Brooklyn, N. H.
Burns, G. H., Central Islip, N. Y.
Burrage, Thomas J., Portland, Me.
Butler, Glent. R., Brooklyn, N. Y.
Byrne, Jos. Henry, New York City.

Caillé, August, New York City, N. Y.
Calvert, W. J., Dallas, Tex.
Carman, Albro R., New York City.
Cassidy, John M., Jersey City, N. J.
Chapin, Edward, Brooklyn, N. Y.
Christie, Arthur C., Corry, Pa.
Churchill, Jas. F., San Diego, Cal.
Clark, Ramond, Brooklyn, N. Y.
Cohen, Bernard, Buffalo, N. Y.
Collins, Danl. W., Wilkes-Barre, Pa.
Conklin, C. B., Washington, D. C.
Connolly, Richard N., Newark, N. J.
Connor, Guy L., Detroit, Mich.
Conway, F. C., Albany, N. Y.
Cooper, W. G., Ogdensburg, N. Y.
Corbus, B. R., Grand Rapids, Mich.
Cornwall, E. E., Brooklyn, N. Y.
Coughlin, Robert E., Brooklyn, N. Y.
Coulter, F. E., Omaha, Neb.
Crafts, Leo M., Minneapolis, Minn.
Cramp, Arthur J., Chicago, Ill.
Croftan, Alfred C., Chicago, Ill.
Cruikshank, Wm. J., Brooklyn, N. Y.
Cullings, Jesse J., Memphis, Tenn.
Cummings, Rol., Los Angeles, Cal.
Curtis, Grant P., Union, N. J.
Cutter, William W., Peoria, Ill.

Daland, Judson, Philadelphia, Pa.
Dattelbaum, M. J., Brooklyn, N. Y.
Davin, John P., New York City.
Dawes, Spencer L., New York City.
De Buys, L. R., New Orleans, La.
De Lorme, M. F., Brooklyn, N. Y.
Dercum, Francis X., Phila., Pa.
De Yoanna, A., Brooklyn, N. Y.
Dickinson, H. S., Philadelphia ,Pa.
Diner, Jacob, New York City, N. Y.
Dill, George H., Utica, N. Y.
Dobkin, Nicholas, Brooklyn, N. Y.
Donovan, Daniel J., New York City.
Dowd, Ambrose F., Newark, N. J.
Dowden, C. W., Louisville, Ky.
Dunklin, F. B., Nashville, Tenn.

Eckel, John L., Buffalo, N. Y.
Edson, David Orr, New York City.
Egan, Cornelius J., New York City.
Eichler, Philip, Bronx, New York.
Elliott, Daniel, Newark, N. J.
Evans, Britton D., Greystone, N. J.
Evans, George A., Brooklyn, N. Y.

Fairbairn, Henry A., Brooklyn, N. Y.
Fassett, Chas. W., Kansas City, Mo.
Faust, Louis, Schenectady, N. Y.
Field, C. Everett, New York City.
Finck, T. D., Louisville, Ky.
Fishbaugh, E. C., Los Angeles, Cal.
Fisher, Charles M., Brooklyn, N. Y.

Fisher, E. M., Greystone Pk., N. J.
Flagge, Fredk. W., Rockaway, N. J.
Fleischaker, F. W., Louisville, Ky.
Fliedner, G. B., Cleveland, O.
Fontaine, Bryce W., Memphis, Tenn.
Friedman, G. A., New York City.
Friend, John M., Cleveland, O.
Fuller, Frank M., Keokuk, Ia.
Futterer, Gus. A., Chicago, Ill.

Gaertner, Fredk., Pittsburgh, Pa.
Gehring, E. W., Portland, Me.
George, S., Pittsburgh, Pa.
Gerin, John, Auburn, N. Y.
Gibson, Arthur R., Buffalo, N. Y.
Gilfillan, W. White., New York City.
Goddard, W. W., Schenectady, N. Y.
Gompertz, L. M., New Haven, Conn.
Gordon, Alfred, Philadelphia, Pa.
Gordon, Murray B., Brooklyn, N. Y.
Gottlieb, Charles, New York City.
Gould, L. A., Schenectady, N. Y.
Grandy, Charles R., Norfolk, Va.
Granger, Frank B., Boston, Mass.
Graves, M. L., Galveston, Tex.
Graves, Nathaniel A., Chicago, Ill.
Grayson, Cary T., Washington, D. C.
Grayson Thos. W., Pittsburgh, Pa.
Gray, T. N., East Orange, N. J.
Greeff, J. G. Wm., New York City.
Greene, Chas. L., St. Paul, Minn.
Greiwe, John E., Cincinnati, O.
Griswold, Alex. V., Louisville, Ky.
Gutman, J., Brooklyn, N. Y.

Hall, Josiah N., Denver, Colo.
Halpern, J., New York City, N. Y.
Haass, E. W., Detroit, Mich.
Ham, Still., S., Schenectady, N. Y.
Hamilton, H. D., Kansas City, Mo.
Hangarter, And. H., Brooklyn, N. Y.
Harrison, Bev. Drake, Detroit, Mich.
Hatch, J. Leffing'll, New York City.
Head, Geo. D., Minneapolis, Minn.
Heller, Jos. M., Washington, D. C.
Hemmeter, John C., Baltimore, Md.
Henderson, Max, Louisville, Ky.
Henschel, L. K., Greystone Pk., N. J.
Heussy, Wm. C., Seattle, Wash.
Hiatt, Houston B., High Point, N. C.
Hickey, Preston M., Detroit, Mich.
Hill, Eben C., Poughkeepsie, N. Y.
Hodges, Fred M., Richmond, Va.
Hodges, J. Allison, Richmond, Va.
Hoff, Peder A., St. Paul, Minn.
Hollis, A. Wm., New York City.
Hollister, Frank C., New York City.
Horine, Emmet F., Louisville, Ky.
Horowitz, Philip, New York City.
Hoxsie, Edward H., Brooklyn, N. Y.
Hubbard, W. S., Brooklyn, N. Y.
Hunt, Edward L., New York City.
Hunter, Geo. G., Los Angeles, Cal.

Irwin, J. W., Louisville, Ky.
Ives, Augustus W., Detroit, Mich.
Ives, Robert F., Brooklyn, N. Y.

Jackson, Algernon B., Phila., Pa.
Jackson, Edw. W., Rochester, N. Y.
Jager, Thor, Wichita, Kan.
Jelly, Arthur C., Boston, Mass.
Jenkins, Wm. A., Louisville, Ky.
Jennings, C. G., Detroit, Mich.
Johnston, George C., Pittsburgh, Pa.
Johnston, J. I., Pittsburgh, Pa.
Jonah, Wm. E., Atlantic City, N. J.
Jones, Allen A., Buffalo, N. Y.
Jones, Clement R., Pittsburgh, Pa.
Jones Frank A., Memphis, Tenn.
Jutte, Max Ernest, New York City.

Katzenbach, W. H., New York City.
Kaufman, Albert, Wilkes-Barre, Pa.
Kaufman, F. J., Syracuse, N. Y.
Kaufman, Jacob, New York City.
Kauffman, Lesser, Buffalo, N. Y.
Kelly, Thomas, New York City.
Kerr, Le Grand, Brooklyn, N. Y.
Keyes, F. P., Brooklyn, N. Y.
Kiefer, Guy S., Detroit, Mich.
King, George W., Secaucus, N. J.
King, Samuel T., Brooklyn, N. Y.
Kiser, Edgar F., Indianapolis, Ind.
Klein, Abraham, Brooklyn, N. Y.
Knapp, Philip C., Boston, Mass.
Krafft, Jacob C., Chicago, Ill.
Kraker, David A., Newark, N. J.
Laporte, Geo. L., New York City.
Lappeus, J. C. S., Binghamton, N. Y.
Lath, Eugene M., Rochester, N. Y.
Lee, John, Detroit, Mich.
Lee, Thomas S., Washington, D. C.
Levy, I. Harris, Syracuse, N. Y.
Levy, I. J., New York City, N. Y.
Levy, Louis H., New Haven, Conn.
Le Wald, Leon T., New York City.
Lewi, Emily, New York City, N. Y.
Lewis, H. Edwin, New York City.
Lichty, John A., Pittsburgh, Pa.
Litchfield, Lawrence, Pittsburgh, Pa.
Little, George F., Brooklyn, N. Y.
Loewenburg, Saml. A., Phila., Pa.
Louria, Leon, Brooklyn, N. Y.
Love, F. W. Buffalo, N. Y.
Love, Wm. S., Baltimore, Md.
Loveland, B. C., Syracuse, N. Y.
Lowrey, James H., Newark, N. J.
Lucas, C. G., Louisville, Ky.
Ludlum W. D., Brooklyn, N. Y.
Lynch, John C., Bridgeport, Conn.
Lytle, Albert T., Buffalo, N. Y.

Magruder, W. Edw., Baltimore, Md.
Maier Otto, New York City, N. Y.
Mallory, Wm. J., Washington, D. C.
Mannheimer, George, New York City.
Martland, Harrison S., Newark, N J.
Matson, Ralph C., Portland, Ore.
Mayer, Edw. E., Pittsburgh, Pa.
Mayhew, John Mills, Lincoln, Neb.
Meling, Nelson C., Chicago, Ill.
Meltzer, Victor, New York City.
Mercur, Wm. H., Pittsburgh, Pa.
Meuer, S. H., New York City, N. Y.
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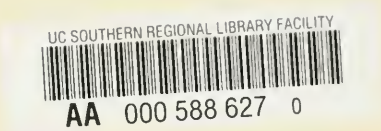
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